

U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

ATTORNEY'S DOCKET NUMBER

446.001

TRANSMITTAL LETTER TO THE UNITED STATES
DESIGNATED/ELECTED OFFICE (DO/EO/US)
CONCERNING A FILING UNDER 35 U.S.C. 371

U.S. APPLICATION NO. (If known, see 37 CFR 1.5

09/786880

INTERNATIONAL APPLICATION NO.

PCT/EP99/07376

INTERNATIONAL FILING DATE

September 13, 1999

PRIORITY DATE CLAIMED

September 11, 1998

TITLE OF INVENTION ESSENTIAL GENES FROM C. ALBICANS AND A METHOD FOR
SCREENING ANTIMYCOTIC SUBSTANCES USING SAID GENES

APPLICANT(S) FOR DO/EO/US


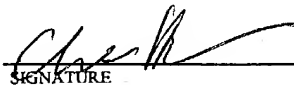
LALANNE et al

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☐ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
 - a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau). in English
 - b. ☐ has been transmitted by the International Bureau.
 - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
 - a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
 - b. ☐ have been transmitted by the International Bureau.
 - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
 - d. ☐ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). (UNEXECUTED)
10. ☐ A translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☐ A FIRST preliminary amendment.
☐ A SECOND or SUBSEQUENT preliminary amendment.
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☒ Other items or information: PCT/RO/101; PCT/IB/306; PCT/IPEA/401;
International Preliminary Examination Report;
Papers to the International Depositary
Authority (8 pages in English; 9 pages in French)
Drawings (9 sheets); Sequence Listing (83 sheets)

U.S. APPLICATION NO. (if known, see 37 CFR 1.53) 09/786880		INTERNATIONAL APPLICATION NO. PCT/EP99/07376		ATTORNEY'S DOCKET NUMBER 446.001	
17. <input checked="" type="checkbox"/> The following fees are submitted:				CALCULATIONS PTO USE ONLY	
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):				\$1000.00	
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO \$1070.00					
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO \$930.00					
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO \$790.00					
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) \$720.00					
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) \$98.00					
ENTER APPROPRIATE BASIC FEE AMOUNT =				\$1000.00	
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).				\$	
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	\$ 414.00	
Total claims	43 - 20 =	23	x 18	\$	
Independent claims	10 - 3 =	7	x 80	\$ 560.00	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ \$270.00	\$	
TOTAL OF ABOVE CALCULATIONS =				\$	
Reduction of 1/2 for filing by small entity, if applicable. A Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28).				+	
SUBTOTAL =				\$1974.00	
Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				\$	
TOTAL NATIONAL FEE =				\$1974.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property +				\$	
TOTAL FEES ENCLOSED =				\$1974.00	
				Amount to be refunded:	\$
				charged:	\$
a. <input checked="" type="checkbox"/> A check in the amount of \$ <u>1974.00</u> to cover the above fees is enclosed.					
b. <input type="checkbox"/> Please charge my Deposit Account No. _____ in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.					
c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. <u>02-2275</u> A duplicate copy of this sheet is enclosed.					
NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.					
SEND ALL CORRESPONDENCE TO:					
Charles A. Muserlian Bierman, Muserlian and Lucas 600 Third Avenue New York, NY 10016					
					
20311 PATENT, TRADEMARK OFFICE					
					
Charles A. Muserlian NAME					
19,683 REGISTRATION NUMBER					

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09/786880

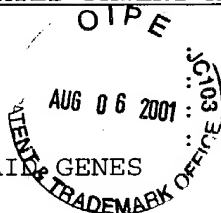
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Rec'd PCT/PTO 06 AUG 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
JEAN-LOUIS LALANNE et al
Serial No.: 09/786,880
Filed: March 8, 2001
For: ESSENTIAL GENES...SAID GENES



600 Third Avenue
New York N.Y. 10016
August 6, 2001

AMENDMENT

Asst. Commissioner for Patents
Washington, D.C. 20231

Sir:

Please amend this application as follows:

IN THE SPECIFICATION:

Page 3, rewrite the second paragraph as follows:

--According to another aspect, the present invention concerns a polynucleotide having the sequence as depicted in SEQ ID No. 2, SEQ ID No. 5, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 13. SEQ ID No. 15, SEQ ID No.17, SEQ ID No. 20, preferably SEQ ID No. 2, SEQ ID No. 5, SEQ ID No. 8, SEQ ID No. 13, SEQ ID No. 14 or SEQ ID No. 17, homologs thereof and functional fragments thereof.--

Replace pages 32 to 37 and 39 with the replacement pages filed herewith.

03/13/2001 HKAYPASH 00000029 09786880

01 FC:116

390.00 OP

IN THE CLAIMS:

Claim 1 (amended) A polynucleotide having the sequence as depicted in the sequence selected from the group consisting of SEQ ID No. 2, SEQ ID No. 5, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 13,

SEQ ID No. 15, SEQ ID No. 17 or SEQ ID No. 20, homologs thereof and functional fragments thereof.

REMARKS


The present amendment is being filed in order to amend the specification in accordance with the floppy disk with the sequences filed herewith. The floppy disk was not generated in the same way the sequences were generated at the time of filing the PCT application. For the genes encoding the protein, the PCT provides the "subsequences". Therefore, a shift had to occur and the diskette filed herewith contains the sequences generated using the proper software. The following table gives the correspondence between the sequences and the specification and claims have been amended accordingly.

SEQ ID No. in PCT Publication	SEQ No. in Electronic Sequence Listings	SEQ ID No. in PCT Publication	SEQ No. in Electronic Sequence Listings
1	1	10	15
2	2	11	17
3	4	12	19
4	5	13	20
5	7	14	22
6	8	15	23
7	10	16	24
8	12	17	25
9	13		

Applicants are submitting herewith a hard copy of the sequence listing as well as the computer readable form (CRF) of the sequence listing. The contents of the paper sequence listing and the computer readable form are the same and where applicable, include no new matter as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b) or 1.825(d).

Respectfully submitted,
Bierman, Muserlian and Lucas

By:


Charles A. Muserlian #19,683
Attorney for Applicants
Tel.# (212) 661-8000

CAM:ds
Enclosures

According to another embodiment of the method of the invention said functional similar genes are essential genes from Candida Spp., preferably Candida albicans, or from Aspergillus Spp., preferably from Aspergillus fumigatus.

According to another aspect, the present invention concerns a polynucleotide having the sequence as depicted in SEQ ID No.2, SEQ ID No.⁵4, SEQ ID No.⁸5, SEQ ID No.¹⁰7, SEQ ID No.¹³9, SEQ ID No.¹⁵10, SEQ ID No.¹⁷11 or SEQ ID No.²⁰12, preferably SEQ ID No.2, SEQ ID No.⁵4, SEQ ID No.⁸5, SEQ ID No.¹³9, SEQ ID No.¹⁵10 or SEQ ID No.¹⁷11, homologs thereof and functional fragments thereof.

According to another aspect, the present invention concerns a gene which is CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, preferably CaOR110, CaMR212, CaNL256, CaBR102 or CaIR012, or a functionally similar gene or a functional fragment thereof.

According to this embodiment, the functionally similar gene or homologous polynucleotide has a sequence identity, at the nucleotide level, with CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, respectively, of at least 50%, preferably of at least 60%, and most preferably of at least 70%. A functional fragment is a polynucleotide fragment that will retain the functionality of the starting product (nucleotide or gene). One example is the CaOR110 splice variant (which is also homologous to the original gene, with about 90% identity).

According to another embodiment, the functionally similar gene has a sequence identity, at the amino-acid level, with CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, respectively, encoded protein(s) of at least 40%, preferably of at least 50%, more preferably of at least 60% and most preferably of at least 70%.

Example 2 : CaBR102

The Internet site of Stanford
(<http://candida.stanford.edu/>) give access to preliminary
sequences of the genome of *C. albicans*. One of these
5 sequences has homology with the YBR102 gene of
S.cerevisiae. Two oligonucleotides were selected in this
sequence (5'-AGTATTCAATTGGGTATTCC-3' and 5'-
CCGGCATCATCAGTAACTCC-3') in order to amplified the
corresponding fragment of *C. albicans*. After cloning, we
10 obtained a sequence of 647 bp (SEQ ID NO: ⁴3). The deduced
protein was compared with the one of YNL102, evidencing 35%
similarity and 26% identity (fig.2). This fragment was
amplified using Pfu polymerase (Stratagene). The PCR
product was purified (High Pure PCR Product Purification
15 Kit, Boehringer Mannheim) and used as a probe for screening
a *C. albicans* genomic DNA library. The latter was prepared
by partial digestion of *C. albicans* genomic DNA with
SauIIIA and cloning into the YEP-24Trp1 vector at the BamHI
restriction site. 40,000 clones of the library were then
20 spread at a density of 2000 clones per dish. Each dish was
covered by a nitrocellulose filter (Membrane Hybond N',
Amersham) which was then successively treated with : 1.5 M
NaCl/0.5 M NaOH, 5 minutes; 1.5 M NaCl/0.5 M Tris-HCl pH
7.2/1 mM EDTA, 3 minutes, twice; DNA was crosslinked to the
25 filters (Amersham Life Science, ultra violet crosslinker).
The probe (100 ng) was labelled with ³²P using the
RediPrime kit and dCTP (Amersham Life Science). The filters
were hybridized in a buffer containing 30% formamide, 5 x
SSC, 5% Denhart's solution, 1% SDS, 100 µg /ml salmon sperm
30 DNA and a probe concentration of 10⁶ cpm/ml at 42°C for 16
h. The membranes were then washed three times at room
temperature in 2 x SSC/0.1% SDS for 5 minutes each and
three times in 1 x SSC/0.1% SDS at 60°C for 20 minutes
each. the filters were then exposed overnight to an X-ray

film. The colonies corresponding to the positives clones were isolated and screened a second time by the same procedure. Two positives clones were finally obtained, which were sequenced on an ABI377 apparatus. the sequences
5 were compiled using ABI software and then analysed using the GCG software package. The nucleotide sequences of these two clones were identical and contained the complete coding sequence corresponding to the probe used, this gene was called CaBR102, whose sequence is represented in SEQ ID
10 No:4. The translation of this nucleotide sequence was examined, account was taken of the fact that in *C. albicans* the CTG codon is translated to serine (there are 3 CTG codons in CaBR102). The deduced protein has 24% identity to *S. cerevisiae* gene YBR102.

15 Example 3 : CaIR012

Chromosomal DNA from the *C. albicans* strain Caf2-1 was isolated using Yeast Cell Lysis prep Kit and Genome DNA Kit from BIO101. A 343 bp fragment from *C. albicans* genomic DNA (SEQ ID NO:5) was amplified with the oligonucleotide
20 primers CaYIR012-5' (5'-GACGTCGTAGACGATACTCAAGAAG-3') and CaYIR012-3' (5'-CTGCAGTAAACCCTCCAGATATAACAG-3') by PowerScript DNA polymerase (PAN Systems GmbH) using the hot start technique. The PCR product was purified from the agarose gel and labeled with fluorescein (Gene image random
25 prime labelling module, Amersham Life Science) according to the manufacturer's instructions. Plasmid DNA from *E.coli* was isolated using Qiagen columns as recommended by the manufacturer. Screening the λ ZAPII *C. albicans* cDNA library was performed following the manufacturer's
30 instructions (Stratagene Ltd.). Nylon filters (Schleicher&Schuell) were lifted from LB-plates (150 mm) with 15000 pfu/plate, denatured 5 min in 1.5M NaCl, 0.5M NaOH, neutralized 3 min in 1.5M NaCl, 0.5M Tris-HCl pH8.0, washed 2 min in 0.2 M Tris-HCl pH 7.5, 2xSSC and DNA was

crosslinked to the filters (Stratagene UV crosslinker). The filters were prehybridized 4 h at 60 °C and hybridized with the fluorescein-labeled DNA probe overnight at 60 °C. Detection was performed with Anti-fluorescein AP conjugate (Signal amplification module for the FluorImager, Amersham LIFE SCIENCE) and analysed after 20 h with a Fluorimager (Storm 860, Molecular Dynamics). Positive plaques were picked and incubated with 0.5 ml SM-buffer (100mM NaCl, 8 mM MgSO₄, 50 mM Tris-HCl pH7.5, 0,01% gelatin). The selected clones were diluted, titered with host cells XL1-Blue and screened and purified a second time by the same procedure. Finally, the pBluescript SK(-) phagemid containing the DNA insert of interest was rescued by the ExAssist Helper Phage system according to the Stratagene protocol. From a total of 75000 screened plaques, 3 positive clones were identified. pBluescript SK (-) phagemid DNA was isolated, sequenced with T3 and T7 primers and the sequences were extended with custom-synthesized oligonucleotide primers. Nucleotide sequence analyses were performed with the Gene Data software package (Gene Data AG, Basel Switzerland). Similarity searches with the Swissprot database were conducted with the BLAST program (Gish, Warren and David J. States (1993). Identification of protein coding regions by database similarity search. Nat. Genet. 3:266-72.). One of these three clones turned out to contain the complete coding sequence corresponding to the probe used; this gene was called CaIR1012, whose sequence is represented in SEQ ID NO: 8.

Example 4: CaJL039

The CaJL039 sequence is depicted in SEQ ID No 7.

The CaJL039 gene was cloned based on gene fragment data issued from the public Stanford Candida albicans sequencing database.

(a) A fragment that showed homology to *Saccharomyces cerevisiae* YJL039c was identified, the sequence of which is given in SEQ ID No ¹²8.

Using the procedure disclosed in example 3 with the
 5 oligonucleotide primer pair (Ca039s: TAG CTC AAC CTA CCA CCA ATC /Ca039r: ATC ACA AGA CTG TCA ATG TAA AT), a short PCR fragment (234 base pairs long) was amplified for screening a *Candida albicans* cDNA lambda ZAP II library (gift of Alistair Brown, Aberdeen).

10 Three positive clones of the 3' coding region were obtained. (# 21t7, 11t3, 21t3).

(b) 3'- and 5'- extension of the internal fragment using the primer walking method

The Sanglard genomic *Candida* DNA library with the
 15 YEp24 vector backbone was used for further amplification of 3'- and 5'-coding sequences. Amplification was carried out by using the following vector-specific oligonucleotide primers and CaJL039 fragment-specific primers:

cggaattcctatcgactacgcgatcatgg: YEp24for (vector
 20 specific)
 gcgaattccgatataggcgccagcaac: YEp24ba (vector specific)
 caattgctttgactcgggtgttattaagt: Ca039-51 (CaJL039: 5'fishing)
 25 tcttggcacaacttgataagaatctgt: Ca039-52 (~)
 taggtgtacgcgaaagccaagtagaac: Ca039-53 (~)
 ttgttaatcgtacacctaaggtgttgac: Ca039-31 (CaJL039: 3'fishing)
 ttgcagattgatgctagcaatgtatttg: Ca039-32 (~).

30 Using the technique of primer walking, the complete 5'-sequence could be amplified (clone 14b-1-1 and clone 17b-3-4).

The missing 3'-sequence was available from GTC PathoGenome Release 5.0, contig #2830.

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An interacting protein (C82, component for RNA polymerase III in yeast) has been identified.

Example 5: CaOR110

5.1. CaOR110

5 The CaOR110 sequence is depicted in SEQ ID No. 9.

CaOR110 was cloned based on gene fragment data issued from the public Stanford *Candida albicans* sequencing database.

10 (a) A small ScOR110-homologous fragment was used in a hybridization experiment to identify CaOR110 clones in a *Candida Albicans* lambda ZAPII cDNA library (from Alistair Brown). Alignment of *Candida Albicans* CaOR110 sequence with the fragment used for hybridization is given in figure 3. The homologous fragment sequence is given in SEQ ID No. 17.

(b) 3'- and 5'- Extension of the internal fragment:

The Sanglard genomic *Candida* DNA library (received from RMV) in the YEP24 vector backbone was used for the amplification of 3'- and 5'- coding and non-coding sequences. This amplification was done by using the vector-specific oligos (directional towards the insert) and CaOR110 fragment-specific oligos (directional towards the vector flanking sequences) described below:

25 cggaattcctatcgactacgcatcatgg : YEP24for
gcgaattccgatataggcgccagcaac : YEP24ba
cgggatccggttaaccaattggatctataaccgtg : 110-ba-150
gcggatcctggtgcccttggtggtgaatg : CaYOR110A
gcggatccctcacaatatgacgattgaaact : CaYOR110B
ggcgtcgactcaggcgccagttttacgtacttcaaattcatc : CaYOR110C
30 tgtgaattcttgacacagggtga : CaYOR110D
caaaccttcagcacaactcca : CaYOR110E,

The finally assembled sequence that included also 3'- and 5'- non-coding sequences was verified by sequencing. The coding region was subcloned into the p414RSGALL-vector.

The map is depicted in Fig. 4.

The homologous yeast ORF (YOR110w) has been described as the transcription factor subunit TFC7 interacting with TFC1 in the TFIIIC polymerase complex (Manaud et al., 1998, Mol. Cell. Biol. 18; 3191-3200).

5.2. CaOR110 splice variant

For CaOR110, an additional splice variant was identified. The clones for the splice variant of CaOR110 were obtained from a *Candida albicans* cDNA library.

10 The sequence is depicted in SEQ ID No. ¹⁵~~10~~.

The splice variant uses the donor site "gtacgt" at position 907 of the original CaOR110 sequence. Acceptor site is at 1047. The map is disclosed in Fig. 5.

15 The alignment of the original CaOR110 and the splice variant is given in fig. 6.

Example 6 : CaMR212

The CaMR212 sequence is depicted in SEQ ID No. ¹⁷~~11~~.

(a) CaMR212 was cloned based on gene fragment data from the public Stanford *Candida albicans* sequencing database.

20 The sequence of a fragment showing homology (Blast search) to the *Saccharomyces cerevisiae* gene YMR212c is given in SEQ ID ¹⁸~~12~~.

25 Based on these data, the following oligos were designed that allow amplification of this fragment (490 bp-fragment) from genomic *Candida albicans* DNA.

Oligos:

CaYMR212for: 5'- cacctgtgaacaacccaccatc-3'

CaYMR212back: 5'- gaatatacctttttaactcaagag -3'

30 (b) 3'- and 5'- extension of this internal fragment from CaMR212

For this purpose, genomic *Candida* DNA libraries from Dominique Sanglard (received from RMV) were used. The YEp24 backbone of this library was used to amplify the 3'- and 5'- coding and non coding sequences with PCR. This was done

by microscope analysis of YMR212-GFP fusion proteins and by biochemical analysis of YMR212-GST fusion proteins).

Example 7 : CaDR325

The CaDR325 sequence is given at SEQ ID ²⁰~~13~~.

5 CaDR325 was cloned based on gene fragment data from the public Stanford *Candida albicans* sequencing database.

(a) 3 fragments that showed homology to *Saccharomyces cerevisiae* YDR325 were identified, the sequences of which are disclosed in SEQ ID ^{12 23 24}~~14~~, ~~15~~ and ~~16~~.

10 Based on these data, the following oligos were designed that allowed the verification of the database sequences and the amplification of an approx. 2200 bp internal CaDR325 fragment from genomic DNA:

cgagcatctacttggttcaaccac: hybCaYDR325ba Oligo
 15 gaatctctggctcgctc: 325-juls Oligo
 gaccgagatacacgagaat: 325-julr Oligo
 ggttaaatacgatcgatgaat: Ca325r Oligo
 caacctcactgacaaatactt: Ca325s Oligo

The finally subcloned 2200 bp internal fragment was
 20 amplified by the combination hybCaYDR325ba + 325-julr oligos.

(c) 3'- and 5'- Extension of the internal fragment:

The Sanglard genomic *Candida* DNA library (received from RMV) in the YEP24 vector backbone was used for the
 25 amplification of 3'- and 5'- coding and non-coding sequences. This was done by using the following vector-specific oligos (directional towards the insert) and CaDR325 2200 bp fragment-specific oligos (directional towards the vector flanking sequences):

30 cggaattcctatcgactacgcatcatgg : YEP24for (vector specific)
 gcgaattccgatataggcgccagcaac : YEP24ba (vector specific)
 acgcttccaatgtattattctcg : Oligo 1-10-A back

CORRECTED PAGES

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Example 2 : CaBR102

The Internet site of Stanford
(<http://candida.stanford.edu/>) give access to preliminary
sequences of the genome of *C. albicans*. One of these
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S.cerevisiae. Two oligonucleotides were selected in this
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CCGGCATCATCAGTAACTCC-3') in order to amplified the
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protein was compared with the one of YNL102, evidencing 35%
similarity and 26% identity (fig.2). This fragment was
amplified using Pfu polymerase (Stratagene). The PCR
product was purified (High Pure PCR Product Purification
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by partial digestion of *C. albicans* genomic DNA with
SauIIIA and cloning into the YEP-24Trp1 vector at the BamHI
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20 spread at a density of 2000 clones per dish. Each dish was
covered by a nitrocellulose filter (Membrane Hybond N⁺,
Amersham) which was then successively treated with : 1.5 M
NaCl/0.5 M NaOH, 5 minutes; 1.5 M NaCl/0.5 M Tris-HCl pH
7.2/1 mM EDTA, 3 minutes, twice; DNA was crosslinked to the
25 filters (Amersham Life Science, ultra violet crosslinker).
The probe (100 ng) was labelled with ³²P using the
RediPrime kit and dCTP (Amersham Life Science). The filters
were hybridized in a buffer containing 30% formamide, 5 x
SSC, 5% Denhart's solution, 1% SDS, 100 µg /ml salmon sperm
30 DNA and a probe concentration of 10⁶ cpm/ml at 42°C for 16
h. The membranes were then washed three times at room
temperature in 2 x SSC/0.1% SDS for 5 minutes each and
three times in 1 x SSC/0.1% SDS at 60°C for 20 minutes
each. the filters were then exposed overnight to an X-ray

film. The colonies corresponding to the positives clones were isolated and screened a second time by the same procedure. Two positives clones were finally obtained, which were sequenced on an ABI377 apparatus. the sequences
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10 No:4. The translation of this nucleotide sequence was examined, account was taken of the fact that in *C. albicans* the CTG codon is translated to serine (there are 3 CTG codons in CaBR102). The deduced protein has 24% identity to *S. cerevisiae* gene YBR102.

15 Example 3 : CaIR012

Chromosomal DNA from the *C. albicans* strain Caf2-1 was isolated using Yeast Cell Lysis prep Kit and Genome DNA Kit from BIO101. A 343 bp fragment from *C. albicans* genomic DNA (SEQ ID NO:7) was amplified with the oligonucleotide
20 primers CaYIR012-5' (5'-GACGTCGTAGACGATACTCAAGAAG-3') and CaYIR012-3' (5'-CTGCACTAAACCCTCCAGATATAACAG-3') by PowerScript DNA polymerase (PAN Systems GmbH) using the hot start technique. The PCR product was purified from the agarose gel and labeled with fluorescein (Gene image random
25 prime labelling module, Amersham Life Science) according to the manufacturer's instructions. Plasmid DNA from *E.coli* was isolated using Qiagen columns as recommended by the manufacturer. Screening the λ ZAPII *C. albicans* cDNA library was performed following the manufacturer's
30 instructions (Stratagene Ltd.). Nylon filters (Schleicher&Schuell) were lifted from LB-plates (150 mm) with 15000 pfu/plate, denatured 5 min in 1.5M NaCl, 0.5M NaOH, neutralized 3 min in 1.5M NaCl, 0.5M Tris-HCl pH8.0, washed 2 min in 0.2 M Tris-HCl pH 7.5, 2xSSC and DNA was

crosslinked to the filters (Stratagene UV crosslinker). The filters were prehybridized 4 h at 60 °C and hybridized with the fluorescein-labeled DNA probe overnight at 60 °C. Detection was performed with Anti-fluorescein AP conjugate (Signal amplification module for the FluorImager, Amersham LIFE SCIENCE) and analysed after 20 h with a Fluorimager (Storm 860, Molecular Dynamics). Positive plaques were picked and incubated with 0.5 ml SM-buffer (100mM NaCl, 8 mM MgSO₄, 50 mM Tris-HCl pH7.5, 0.01% gelatin). The selected clones were diluted, titered with host cells XL1-Blue and screened and purified a second time by the same procedure. Finally, the pBluescript SK(-) phagemid containing the DNA insert of interest was rescued by the ExAssist Helper Phage system according to the Stratagene protocol. From a total of 75000 screened plaques, 3 positive clones were identified. pBluescript SK (-) phagemid DNA was isolated, sequenced with T3 and T7 primers and the sequences were extended with custom-synthesized oligonucleotide primers. Nucleotide sequence analyses were performed with the Gene Data software package (Gene Data AG, Basel Switzerland). Similarity searches with the Swissprot database were conducted with the BLAST program (Gish, Warren and David J. States (1993). Identification of protein coding regions by database similarity search. Nat. Genet. 3:266-72.). One of these three clones turned out to contain the complete coding sequence corresponding to the probe used; this gene was called CaIR1012, whose sequence is represented in SEQ ID NO:8.

Example 4: CaJL039

The CaJL039 sequence is depicted in SEQ ID No 7.

The CaJL039 gene was cloned based on gene fragment data issued from the public Stanford *Candida albicans* sequencing database.

(a) A fragment that showed homology to *Saccharomyces cerevisiae* YJL039c was identified, the sequence of which is given in SEQ ID No12.

Using the procedure disclosed in example 3 with the
 5 oligonucleotide primer pair (Ca039s: TAG CTC AAC CTA CCA
 CCA ATC /Ca039r: ATC ACA AGA CTG TCA ATG TAA AT), a short
 PCR fragment (234 base pairs long) was amplified for
 screening a *Candida albicans* cDNA lambda ZAP II library
 (gift of Alistair Brown, Aberdeen).

10 Three positive clones of the 3' coding region were
 obtained. (# 21t7, 11t3, 21t3).

(b) 3'- and 5'- extension of the internal
 fragment using the primer walking method

The Sanglard genomic *Candida* DNA library with the
 15 YEp24 vector backbone was used for further amplification of
 3'- and 5'-coding sequences. Amplification was carried out
 by using the following vector-specific oligonucleotide
 primers and CaJL039 fragment-specific primers:

cggaattcctatcgactacggatcatgg: YEp24for (vector
 20 specific)
 gcgaattccgatataggcgccagcaac: YEp24ba (vector
 specific)
 caattgctttgactcgggtgttattaagt: Ca039-51 (CaJL039:
 5'fishing)
 25 tcttggcacaacttgataagaatctgt: Ca039-52 (~)
 taggtgtacgcgaaagccaagtagaac:Ca039-53 (~)
 ttgttaatcgtacacctaaggtgttgac: Ca039-31 (CaJL039:
 3'fishing)
 ttgcagattgatgctagcaatgtatttg: Ca039-32 (~).

30 Using the technique of primer walking, the complete
 5'-sequence could be amplified (clone 14b-1-1 and clone
 17b-3-4).

The missing 3'-sequence was available from GTC
 PathoGenome Release 5.0, contig #2830.

An interacting protein (C82, component for RNA polymerase III in yeast) has been identified.

Example 5: CaOR110

5.1. CaOR110

5 The CaOR110 sequence is depicted in SEQ ID No. 13.

CaOR110 was cloned based on gene fragment data issued from the public Stanford *Candida albicans* sequencing database.

(a) A small ScOR110-homologous fragment was used in a hybridization experiment to identify CaOR110 clones in a *Candida Albicans* lambda ZAPII cDNA library (from Alistair Brown). Alignment of *Candida Albicans* CaOR110 sequence with the fragment used for hybridization is given in figure 3. The homologous fragment sequence is given in SEQ ID No. 25.

(b) 3'- and 5'- Extension of the internal fragment:

The Sanglard genomic *Candida* DNA library (received from RMV) in the YEP24 vector backbone was used for the amplification of 3'- and 5'- coding and non-coding sequences. This amplification was done by using the vector-specific oligos (directional towards the insert) and CaOR110 fragment-specific oligos (directional towards the vector flanking sequences) described below:

cggaattcctatcgactacgcatcatgg : YEP24for
 25 gcgaattccgatataggcgccagcaac : YEP24ba
 cgggatccggtaaccaattggatctataaccgtg : 110-ba-150
 gcggatcctggtgcccttggtggtgaatg : CaYOR110A
 gcggatccctcacaatatgacgattgaaact : CaYOR110B
 ggcgtcgactcaggcgccagttttacgtacttcaaattcatc : CaYOR110C
 30 tgtgaattcttgacacagggtga : CaYOR110D
 caaaccttcagcacaactcca : CaYOR110E

The finally assembled sequence that included also 3'- and 5'- non-coding sequences was verified by sequencing. The coding region was subcloned into the p414RSGALL-vector.

The map is depicted in Fig. 4.

The homologous yeast ORF (YOR110w) has been described as the transcription factor subunit TFC7 interacting with TFC1 in the TFIIIC polymerase complex (Manaud et al., 1998, Mol. Cell. Biol. 18; 3191-3200).

5.2. CaOR110 splice variant

For CaOR110, an additional splice variant was identified. The clones for the splice variant of CaOR110 were obtained from a *Candida albicans* cDNA library.

10 The sequence is depicted in SEQ ID No.15.

The splice variant uses the donor site "gtacgt" at position 907 of the original CaOR110 sequence. Acceptor site is at 1047. The map is disclosed in Fig. 5.

15 The alignment of the original CaOR110 and the splice variant is given in fig. 6.

Example 6 : CaMR212

The CaMR212 sequence is depicted in SEQ ID No.17.

(a) CaMR212 was cloned based on gene fragment data from the public Stanford *Candida albicans* sequencing database.

20 The sequence of a fragment showing homology (Blast search) to the *Saccharomyces cerevisiae* gene YMR212c is given in SEQ ID, 19.

Based on these data, the following oligos were designed that allow amplification of this fragment (490 bp-fragment) from genomic *Candida albicans* DNA.

Oligos:

CaYMR212for: 5'- cacctgtgaacaacccaccatc-3'

CaYMR212back: 5'- gaatatacctttttaactcaagag -3'

25 (b) 3'- and 5'- extension of this internal fragment from CaMR212

For this purpose, genomic *Candida* DNA libraries from Dominique Sanglard (received from RMV) were used. The YEp24 backbone of this library was used to amplify the 3'- and 5'- coding and non coding sequences with PCR. This was done

by microscope analysis of YMR212-GFP fusion proteins and by biochemical analysis of YMR212-GST fusion proteins).

Example 7 : CaDR325

The CaDR325 sequence is given at SEQ ID 20.

5 CaDR325 was cloned based on gene fragment data from the public Stanford *Candida albicans* sequencing database.

(a) 3 fragments that showed homology to *Saccharomyces cerevisiae* YDR325 were identified, the sequences of which are disclosed in SEQ ID 22, 23 and 24.

10 Based on these data, the following oligos were designed that allowed the verification of the database sequences and the amplification of an approx. 2200 bp internal CaDR325 fragment from genomic DNA:

cgagcatctacttggttcaaccac: hybCaYDR325ba Oligo

15 gaatctctggctcgctc: 325-juls Oligo

gaccgagatacacgagaat: 325-julr Oligo

ggttaaatgatcgatgatgaat: Ca325r Oligo

caacctcactgacaaatactt: Ca325s Oligo

20 The finally subcloned 2200 bp internal fragment was amplified by the combination hybCaYDR325ba + 325-julr oligos.

(c) 3'- and 5'- Extension of the internal fragment:

25 The Sanglard genomic *Candida* DNA library (received from RMV) in the YEP24 vector backbone was used for the amplification of 3'- and 5'- coding and non-coding sequences. This was done by using the following vector-specific oligos (directional towards the insert) and CaDR325 2200 bp fragment-specific oligos (directional towards the vector flanking sequences):

30 cggaattcctatcgactacgcgatcatgg : YEP24for (vector specific)

gcgaattccgatataggcgccagcaac : YEP24ba (vector specific)

acgcttccaatgtattattctcg : Oligo 1-10-A back

Claims:

1. A polynucleotide having the sequence as depicted
in the sequence selected from the group consisting of SEQ
5 ID No.2, SEQ ID No.⁵4, SEQ ID No.⁸6, SEQ ID No.¹⁰7, SEQ ID
No.¹⁵9, SEQ ID No.¹⁵10, SEQ ID No.¹⁷11 or SEQ ID No.²⁰13, homologs
thereof and functional fragments thereof.

2.-The polynucleotide of claim 1 which is the gene
10 CaNL256, homologs thereof and functional fragments thereof.

3.-The polynucleotide of claim 1 which is the gene
CaBR102, homologs thereof and functional fragments thereof.

15 4.-The polynucleotide of claim 1 which is the gene
CaIR012, homologs thereof and functional fragments thereof.

5.-The polynucleotide of claim 1 which is the gene
CaMR212, homologs thereof and functional fragments thereof.
20

6.-The polynucleotide of claim 1 which is the gene
CaDR325, homologs thereof and functional fragments thereof.

7.-The polynucleotide of claim 1 which is the gene
25 CaOR110, homologs thereof and functional fragments thereof.

8.-The polynucleotide of claim 1 which is the gene
CaJL039, homologs thereof and functional fragments thereof.

30 9 -A protein encoded by the polynucleotide according
to claim 2 or a functional polypeptide fragment thereof.

10 -A protein encoded by the polynucleotide according
to claim 3 or a functional polypeptide fragment thereof.

9/PRTS

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ESSENTIAL GENES FROM C. ALBICANS AND A METHOD FOR
SCREENING ANTIMYCOTIC SUBSTANCES USING SAID GENES

The present invention relates to a method for
5 screening for antimycotic substances in which essential
genes from mycetes, particularly from Candida albicans
(C.albicans) as well as functionally similar genes from
other pathogenic mycetes, or the corresponding encoded
proteins, are used as targets. The invention also relates
10 to specific C. albicans genes.

The spectrum of known fungal infections stretches from
fungal attack of skin or nails to potentially hazardous
mycotic infections of the inner organs; Such infections and
resulting diseases are known as mycosis.

15 Antimycotic substances (fungistatic or fungicidal) are
used for treatment of mycosis. However, up to now,
relatively few substances with pharmacological effects are
known, such as Amphotericin B, Nystatin, Pimaricin,
Griseofulvin, Clotrimazole, 5-fluoro-cytosine and
20 Batraphene. The drug treatment of fungal infections is
extremely difficult, in particular because both the host
cells and the mycetes, are eucaryotic cells. Administration
of drugs based on known antimycotic substances results
therefore often in undesired side-effects, for example
25 Amphotericin B has a nephrotoxic effect. Therefore, there
is a strong need for pharmacologically efficient substances
usable for the preparation of drugs, which are suitable for
prophylactic treatments of immunodepressive states or for
the treatment of an existing fungal infection. Furthermore,
30 the substances should exhibit a specific spectrum of action
in order to selectively inhibit the growth and
proliferation of mycetes without affecting the treated host
organism.

The aim of the present invention is to provide a method for the identification of antimycotic substances and especially for the identification of anti-Candida substances. An essential feature of this method is that
5 essential genes from mycetes are used as targets for the screening.

The present invention thus concerns a method for screening antimycotic substances wherein an essential gene from mycetes or a functionally similar gene in another
10 pathogenic mycete, or the corresponding encoded protein, is used as target and wherein the essential gene is selected from the group consisting of CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 and CaJL039.

According to one embodiment of the method of the
15 invention mycete cells which express the essential gene, or a functionally similar mycete gene, to a different level are incubated with the substance to be tested and the growth inhibiting effect of the substance is determined.

20 According to another embodiment, said target gene or the corresponding target gene encoded protein is contacted in vitro with the substance to be tested and the effect of the substance on the target is determined.

According to another embodiment, the screened
25 substances inhibit partially or totally the functional expression of the essential genes or the functional activity of the encoded proteins.

According to one embodiment the screened substances partially or totally inhibit the activity of
30 dihydropneopterin aldolase (DHNA) and/or dihydropteroate synthase (DHPS) and/or 7,8-dihydro-6-hydroxymethylpterin-pyrophosphokinase (HPPK).

According to another embodiment, the mycete species are selected from the group comprising Basidiomycetes, Ascomycetes and Hyphomycetes.

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According to another embodiment of the method of the invention said functional similar genes are essential genes from *Candida* Spp., preferably *Candida albicans*, or from *Aspergillus* Spp., preferably from *Aspergillus*
5 *fumigatus*.

According to another aspect, the present invention concerns a polynucleotide having the sequence as depicted in SEQ ID No.2, SEQ ID No.4, SEQ ID No.6, SEQ ID No.7, SEQ ID No.9, SEQ ID No.10, SEQ ID No.11 or SEQ ID No.13,
10 preferably SEQ ID No.2, SEQ ID No.4, SEQ ID No.6, SEQ ID No.9, SEQ ID No.10 or SEQ ID No.11, homologs thereof and functional fragments thereof.

According to another aspect, the present invention concerns a gene which is CaOR110, CaMR212, CaNL256,
15 CaBR102, CaIR012, CaDR325 or CaJL039, preferably CaOR110, CaMR212, CaNL256, CaBR102 or CaIR012, or a functionally similar gene or a functional fragment thereof.

According to this embodiment, the functionally similar gene or homologous polynucleotide has a sequence identity,
20 at the nucleotide level, with CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, respectively, of at least 50%, preferably of at least 60%, and most preferably of at least 70%. A functional fragment is a polynucleotide fragment that will retain the functionality of the starting
25 product (nucleotide or gene). One example is the CaOR110 splice variant (which is also homologous to the original gene, with about 90% identity).

According to another embodiment, the functionally similar gene has a sequence identity, at the amino-acid
30 level, with CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, respectively, encoded protein(s) of at least 40%, preferably of at least 50%, more preferably of at least 60% and most preferably of at least 70%.

These figures given for the gene apply mutatis mutandis to the polynucleotide, as far as homology and similarity.

According to another aspect, the present invention covers the protein(s) encoded by CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, respectively, gene(s) or by a functionally similar gene, or a functional polypeptidic fragment thereof.

According to another aspect, the present invention provides a plasmid containing CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, respectively, gene(s), a functionally similar gene or a functional fragment thereof

According to another aspect, the present invention provides a plasmid (bacteria containing same) deposited at the CNCM (Institut Pasteur, Paris) on 98/08/13, with the accession numbers I-2065, I-2063 and I-2064, corresponding to the CaNL256, CaBR102 and CaIR012 genes, respectively.

According to another aspect, the present invention provides a plasmid (bacteria containing same) deposited at the DSMZ (Deutsche Sammlung von Mikroorganismen und Zellkulturen, Germany) on 99/08/06 with the accession numbers DSM 12977, DSM 12976, DSM 12978 and DSM 12979, corresponding to the CaDR325, CaOR110, CaOR110 splice variant and CaMR212, respectively.

According to another aspect, the present invention provides a kit for diagnosis of fungal infections comprising a gene selected from the group consisting of CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 and CaJL039, a functionally similar gene thereof, a functional fragment thereof, the corresponding encoded protein or a functional polypeptide fragment thereof.

According to another aspect, the present invention provides an antibody directed against the protein encoded

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by the CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, respectively, gene(s) or by a functionally similar gene, or a polypeptide fragment thereof.

According to another aspect, the present invention provides a polynucleotide obtainable by the process comprising the following steps:

- (i) selecting an essential gene from *Saccharomyces cerevisiae*;
- (ii) comparing the sequence of said gene with *Candida Albicans* genome sequences;
- (iii) deducing homologous oligonucleotides regions;
- (iv) PCR amplifying the thus-obtained oligonucleotides;
- (v) using the amplimers of step (iv) for detecting the complete gene of interest:

the amplimers of step (iv) are used as a probe for detecting the complete gene of interest from a *Candida albicans* genomic or cDNA library; or

- the complete gene is obtained by 3' and 5' extension of the amplimer, e.g. by using a PCR method.

According to the invention, the first step is to identify said essential genes and starting from these thus identified genes, essential genes from other pathogenic mycetes can be identified. For practical purposes, essential genes from *S. cerevisiae* are first identified and starting from them, essential genes from other pathogenic fungus, especially from *Candida*, are obtained.

The present invention thus discloses the identification of essential genes from *C.albicans* and their use in a method for the screening of antimycotic substances, especially anti-*Candida* substances.

In order to identify essential genes of *S.cerevisiae*, individual genomic genes are eliminated through homologous

recombination. If the DNA segment thus eliminated concerns an essential gene, then the deletion is lethal for the *S.cerevisiae* cells in haploid form.

A method, wherein the studied *S. cerevisiae* gene is replaced by a marker gene can be used to generate the corresponding genomic deletion of *S.cerevisiae* and to determine the *S.cerevisiae* cells containing the deletion.

As a selection marker a dominant selection marker (e.g. kanamycin resistance gene) or an auxotrophic marker can for example be used. As an auxotrophic marker, it is possible to use genes coding for key enzymes of amino acid or nucleic base synthesis. For example, one can use as a selection marker the following genes from *S.cerevisiae* : gene encoding for the metabolic pathway of leucine (e.g.LEU2-gene), histidine (e.g. HIS3-gene) or tryptophan (e.g. TRP-1 gene) or for the nucleic base metabolism of uracil (e.g. URA3-gene).

Auxotrophic *S.cerevisiae* strains can be used. These auxotrophic strains can only grow on nutritive media containing the corresponding amino acids or nucleotide bases. All laboratory *S.cerevisiae* strains, containing auxotrophic markers can for instance be used. When diploid *S.cerevisiae* strains are used, then the corresponding marker gene must be homozygously mutated. Strain CEN.PK2 or isogenic derivatives thereof can be used.

Strains containing no suitable auxotrophic marker can also be used such as prototrophic *S.cerevisiae* strains. Then a dominant selection marker e.g. resistance gene, such as kanamycin resistance gene can be used. A loxP-KanMX-loxP cassette can advantageously be used for this purpose.

For the homologous recombination replacing the whole DNA sequence or part thereof of a *S.cerevisiae* gene, DNA fragments are used wherein the marker gene is flanked at

the 5'- and 3'-ends by sequences which are homologous to the 5'- and 3'-ends of the studied *S.cerevisiae* gene.

Different processes can be used for the preparation of the corresponding DNA fragments which are also appropriate for the deletion of any specific *S.cerevisiae* gene. A linear DNA-fragment is used for the transformation of the suitable *S.cerevisiae* strain. This fragment is integrated into the *S.cerevisiae* genome by homologous recombination. These processes include:

10 1. "Conventional method" for the preparation of deletion cassettes (Rothstein, R.J. (1983) Methods in Enzymology, Vol. 101, 202-211).

2. "Conventional Method" using the PCR technique ("modified conventional method").

15 3. SFH (short flanking homology)- PCR method (Wach, A. et al. (1994) Yeast 10: 1793-1808; Gültner, U. et al. (1996) Nucleic Acids Research 24:2519-2524).

1. In the "conventional method" for the preparation of deletion cassettes in the *S.cerevisiae* genome, the gene to be studied is either already present in an appropriate vector or is integrated in such a vector. With this method, any pBR- pUC- and pBluescript®-derivates can be used for example. A major part of the target gene sequence is eliminated from the vector, for instance using appropriate restriction sites, conserving however the 3'- and 5'- regions of the studied gene inside the vector. The selected marker gene is integrated between the remaining regions.

2. In the modified form of this "conventional method", PCR is used. This method allows amplification of the 3'- and 5'-terminal regions of the coding sequence of the studied *S.cerevisiae* gene. This method amplifies selectively both terminal regions of the studied gene, therefore, two PCR-reactions must be carried out for each studied gene, amplifying once the 5'-end, and once the 3'-

end of the gene. The length of the amplified terminal DNA-fragment depends on the existing restriction sites. The amplified terminal ends of the studied gene have generally a length of 50 to 5000 base pairs (bp), preferably a length
5 between 500 and 1000 bp.

As template for the PCR-reactions, genomic DNA of *S.cerevisiae* or wild-type genes can be used. The primer-pairs (a sense and an antisense primer, respectively) are constructed so that they correspond to the 3'-end and the
10 5'-end sequence of the studied *S.cerevisiae* gene. Especially, the primer is selected such as to allow its integration by way of appropriate restriction sites.

As vectors, pBR- pUC- and pBluescript®-derivates can be used. In particular vectors already containing a gene
15 encoding the selection marker, are appropriate. In particular, vectors can be used, which contain genes of the selection marker HIS3, LEU2, TRP1 or URA3.

The DNA segments of the studied *S.cerevisiae* gene, obtained by PCR, are integrated in the vector at both sides
20 of the selection marker, so that subsequently, as in the "conventional method", the selection marker is flanked on both ends by DNA sequences which are homologous to the studied gene.

3. Homologous recombination in *S.cerevisiae* takes
25 place in a very efficient and precise manner and the length of the DNA sequence homologous to the studied *S.cerevisiae* gene flanking the selection marker gene can in fact be considerably shorter than with the "modified conventional method". The flanking ends homologous to the studied
30 *S.cerevisiae* gene need to present a length of only about 20-60 bp, preferably 30-45 bp. The SFH-PCR method is particularly advantageous as the laborious cloning step can be obviated.

A PCR reaction is carried out on a DNA-template containing the gene for the selection marker to be used, wherein the primers are constructed so that the DNA sequence of the sense primer is homologous to the 5'-end of the selection marker sequence and so that the primer presents in addition at its 5'-end a region of preferably 40 nucleotides, which corresponds to the 5'-terminal sequence of the studied *S.cerevisiae* gene. The antisense primer is constructed in an analogous manner, i.e. it is complementary to the 3'-end of the gene sequence of the selection marker, wherein this primer contains at its 5'-end a region of also preferably 40 nucleotides, which corresponds to the complementary strand of the 3'-terminal coding sequence of the studied gene.

For the amplification of *S.cerevisiae* genes to be studied by the SFH-PCR method, vectors containing the gene for the auxotrophic marker or selection marker can be used. Especially, plasmid pUG6 is used as the template. This plasmid contains a loxP-KanMX-loxP cassette (Gültner, U. et al. (1996) *Nucleic Acids Research* 24: 2519-2524). In other terms, the Kanamycin resistance gene is flanked at both ends by a loxP sequence (loxP-KanMX-loxP cassette). This cassette is advantageous in that the Kanamycin resistance gene can be eventually eliminated from the *S.cerevisiae* genome after integration of the loxP-KanMX-loxP cassette into the *S.cerevisiae* gene to be studied. Cre-recombinase of bacteriophage P1 can be used for this purpose. Cre-recombinase recognizes the loxP sequences and induces elimination of the DNA located between the two loxP sequences by a homologous recombination process. As a result only one loxP sequence remains and the so-called marker regeneration occurs, i.e. the *S.cerevisiae* strain may be transformed again using the loxP-KanMX-loxP cassette. This is particularly advantageous, when at least

two functionally similar genes are to be deleted in order to obtain a lethal phenotype.

With the PCR-method, the PCR reaction primers are at the 3'-end a preferably 20 nucleotide long sequence, which is homologous to the sequence situated left and/or right of the loxP-KanMX-loxP cassette, and at the 5'-end a preferably 40 nucleotide long sequence, which is homologous to the terminal ends of the gene to be studied.

Using the three methods, one obtains linear deletion cassettes containing the gene encoding the selection marker, which is flanked on both sides by homologous sequences of the gene to be studied. The deletion cassettes are used for the transformation of diploid *S.cerevisiae* strains. The diploid strain *S.cerevisiae* CEN.PK2 (Scientific Research & Development GmbH, Oberursel) can be used for example for this purpose.

[CEN.PK2 Mata/MAT α ura3-52/ura3-52 leu2-3, 112/leu2-3, 112his3 Δ 1/his3 Δ 1 trp1-289/trp1-289 MAL2-8^C/MAL2-8^C SUC2/SUC2]

The strain CEN.PK2 is prepared and cultivated using known methods (Gietz, R.D. et al. (1992) Nucleic Acids Research 8: 1425; Güldener, U. et al. (1996) Nucleic Acids Research 24:2519-2524).

The cells of the *S.cerevisiae* strain used are transformed according to known processes with an appropriate DNA quantity of the linear deletion cassette (e.g. Sambrook et al. 1989). Thereafter, the medium in which the cells are cultivated is replaced by a new medium, a so-called selective medium, which does not contain the corresponding amino acid (e. g. histidine, leucine or tryptophan) or nucleic base (e. g. uracil) or, when using a deletion cassette containing the kanamycin resistance gene, by a medium containing geneticin (G418[®]) (e.g. a complete medium (YEPD) containing geneticin). Alternatively, the

transformed cells may be plated on agar plates prepared using the corresponding media. Thereby, one selects the transformed cells, in which a homologous recombination occurred, since only those cells can grow under these
5 modified conditions.

However, in most cases, only one of the two copies of the gene in the double chromosome set of a diploid *S.cerevisiae* strain is replaced by the DNA of the deletion cassette during the transformation, resulting in a
10 heterozygote-diploid *S.cerevisiae* mutant strain, wherein one copy of the gene studied is replaced by a selection marker, while the other copy of the gene is maintained in the genome. This presents the advantage that in case of a deletion of an essential gene, due to the existence of the
15 second copy of the essential gene, the mutant *S.cerevisiae* strain is still viable.

The proper integration of the deletion cassette DNA at the predetermined chromosomal gene locus (gene locus of the gene to be studied) may be checked by Southern-Blot
20 Analysis (Southern, E.M. (1975) J. Mol. Biol. 98:503-517) or by diagnostic PCR analysis using specific primers (Güldener, U. et al. (1996) Nucleic Acids Research 24:2519-2524)

The genetic separation of individual diploid cells may
25 be monitored by tetrad analysis. To this end, reduction division (meiosis) is induced in the diploid cells, especially heterozygote mutant strains, using known methods such as nitrogen impoverishment on potassium acetate plates (Sherman, F. et al. (1986) Cold Spring Harbor Laboratory
30 Press, Cold Spring Harbor, N. Y.; Guthrie, C. and Fink, G.R. (1991) Methods in Enzymology, Vol.194. Academic Press, San Diego, 3-21; Ausubel, F. M. et al. (1987) Current Protocol in Molecular Biology John Wiley and Sons, Inc., Chapter 13). Meiosis results only in asci with four

ascospores (segregated), which can be individualized after partial enzymatic digestion of the ascospore wall with zymolyase (Ausubel et al. (1987)) by way of micromanipulators (e.g. SINGER). For example when a tetrad analysis is carried out on a heterozygote-diploid mutant strain in which an essential gene present in the double chromosome set is replaced on one chromosome by homologous recombination, then only two segregated ascospores are viable, namely those which carry the essential gene. The two remaining segregated ascospores are not viable because they lack the essential gene.

In order to check if the genes studied by this method are really essential or if the homologous recombination leads to an alteration of an essential gene adjacent to the gene locus of the gene studied, the heterozygote diploid *S.cerevisiae* mutant strain is transformed with a centromere plasmid containing said studied gene.

A tetrad analysis is carried out on the transformants. When four instead of two viable segregates are obtained, then the studied gene contained in the centromere plasmid can complement the defect of the two non-viable haploid *S.cerevisiae* cells/mutant strains, which demonstrates that the studied *S.cerevisiae* gene is essential.

Preferably, plasmids present in low copy number, e.g. one or two copies per cell are used as centromere plasmids. For example plasmids pRS313, pRS314, pRS315 and pRS316 (Sijkorski, R. S. and Hieter, P. (1989) Genetics 122: 19-27) or similar plasmids can be used for this purpose. Preferably, the studied genes are integrated in said plasmids including their 3'- and 5'-end non-coding regions.

Individual *S.cerevisiae* genes may be studied using the above-described method, their sequences being totally or partially known. The complete genomic sequence of

S.cerevisiae was made accessible to the public via the WWW (World Wide Web) on April 24, 1996.

Different possibilities exist to have access to the *S.cerevisiae* genomic DNA sequence via the WWW.

5 MIPS (Munich information Centre of Protein Sequence)
Address <http://speedy.mips.biochem.mpg.de/mips/yeast/>

SGD (Saccharomyces Genome Database, Stanford)

Address <http://genome-www.stanford.edu/Saccharomyces>

YPD (Yeast Protein Database, Cold Spring Harbor)

10 Address <http://www.proteome.com/YPDhome.html>

The complete *S.cerevisiae* DNA sequence is also accessible via FTP (file transfer protocol) in Europe (e.g. at the address: [ftp.mips.emblnet.org](ftp://mips.emblnet.org)) in the U.S.A. (address: [genome-ftp.stanford.edu](ftp://genome-ftp.stanford.edu)) or in Japan (address: [ftp.nig.ac.jp](ftp://ftp.nig.ac.jp)).

7 essential genomic *S.cerevisiae* genes have been identified by this way: YDR325w, YJL039c, YOR110w, YNL256w, YBR102c, YIR012w and YMR212c

The essential genes of *S.cerevisiae* are then used to
20 identify corresponding functionally similar genes in other mycetes.

By functionally similar genes in other mycete species, is meant genes which have a function similar or identical to that of the identified essential genes of *S.cerevisiae*.
25 Functionally similar genes in other mycetes may, but need not be homologous in sequence to the corresponding essential *S.cerevisiae* genes. Functionally similar genes in other mycetes may exhibit only moderate sequence homology at the nucleotide level to the corresponding essential
30 *S.cerevisiae* genes. By moderate sequence homology it is meant in the present invention genes having a sequence identity, at the nucleotide level, of at least 50%, more preferably of at least 60% and most preferably of at least 70%.

In addition, functionally similar genes in other mycetes may, but need not encode proteins homologous in sequence to the proteins encoded by the essential *S.cerevisiae* genes. Functionally similar proteins in other mycetes may exhibit moderate protein sequence homology to the proteins encoded by the essential *S.cerevisiae* genes.

By moderate protein sequence homology is meant in the present invention proteins having a sequence identity, at the amino-acid level, of at least 40%, preferably of at least 50%, more preferably of at least 60% and most preferably of at least 70%.

Genes homologous in sequence may be isolated according to known methods, for example via homologous screening (Sambrook, J. et al. (1989) Molecular Cloning Cold Spring Harbor Laboratory Press, N.Y.) or via the PCR technique using specific primers from genomic libraries and/or cDNA libraries of the corresponding mycetes.

According to one embodiment, genes homologous in sequences are isolated from cDNA libraries. In order to find out functionally similar genes in other mycetes, mRNA is isolated from mycete species to be studied according to known methods (Sambrook et al. 1989) and cDNA is synthesized according to known methods (Sambrook et al. 1989; or cDNA synthesis kits, e.g. from STRATAGENE).

The prepared cDNA is directionally integrated in a suitable expression vector.

For example, synthesis of the first cDNA strand may be carried out in the presence of primers having appropriate restriction sites in order to allow a subsequent cloning in the proper orientation with respect to the expression vector promoter. As restriction sites, any known restriction site may be used. As a primer, for instance the following primer, 50 nucleotides long may be used:

5'-GAGAGAGAGAGAGAGAGAGAGAACTAGTXXXXXTTTTTTTTTTTTTTTTTT-

3'

The sequence (X)₆ represents an appropriate restriction site, for example for XhoI.

5 After two-strand synthesis, the cohesive ends of the double stranded cDNA are filled (blunt end) and the cDNA ends are then ligated using a suitable DNA adaptor sequence. The DNA adaptor sequence should contain a restriction site which should be different from the
10 restriction site used in the primer for the synthesis of the first cDNA strand. The DNA adaptor may comprise for example complementary 9- or 13-mer oligonucleotides, whose ends represent the cohesive end of a restriction site. These ends may be for example a EcoRI-site:

15 5' XXXXXGGCACGAG 3'
3' XCCGTGCTC 5'

The single-stranded X in the adaptor sequence represent the cohesive end of a restriction site.

The cDNA provided with corresponding adaptor sequences
20 is then cleaved using restriction endonuclease, whose recognition site was used in the primer for the synthesis of the first cDNA strand, for example XhoI. The cDNA thus obtained would have according to this example 3'-XhoI and 5'-EcoRI protruding ends and could be therefore
25 directionally integrated into an expression vector cleaved with XhoI and EcoRI.

As expression vectors, among others, E. coli/S.cerevisiae shuttle vectors, i.e. vectors usable in E. coli as well as in S.cerevisiae are suitable. Such
30 vectors may then be amplified for instance in E. coli. As expression vectors, those which are present in a high copy number as well as those present in a low copy number in S.cerevisiae cells can be used. For this purpose, for example vectors selected in the group consisting of pRS423

- pRS426 (pRS423, pRS424, pRS425, pRS426) and/or pRS313-pRS316 (pRS313, pRS314, pRS315, pRS316) (Sikorki, R.S. and Hieter, P. (1989) Genetics 122: 19-27; Christianson T. W. et al. (1992) Gene 110: 119-122) are suitable.

- 5 Expression vectors should contain appropriate *S.cerevisiae* promoters and terminators. In case they do not have these elements, the corresponding promoters and terminators are inserted in such a way that a subsequent incorporation of the generated cDNA remains possible.
- 10 Particularly suitable are the promoters of *S.cerevisiae* genes MET25, PGK1, TPI1, TDH3, ADHI, URA3. One may use promoters of the wild-type gene in non modified form as well as promoters which were modified in such a way that certain activator sequences and/or repressor sequences were
- 15 eliminated. As terminators, for example the terminators of the *S.cerevisiae* genes MET25, PGK1, TPI1, TDH3, ADHI, URA3 are suitable.

- According to another embodiment, genes homologous in sequence are isolated from genomic libraries. Genomic DNA
- 20 libraries from mycetes can be prepared according to procedures known (for example as described in Current Protocols in Molecular Biology, John Wiley and Sons, Inc). For example, genomic DNA from mycetes can be prepared using known methods for yeast cell lysis and isolation of genomic
- 25 DNA (for example commercially available kits from Biol01, Inc). The genomic DNA can be partially digested using a restriction enzyme such as Sau3AI and the fragments are size-selected by agarose gel electrophoresis. DNA fragments having for example a size of 5-10kb are then purified by
- 30 classical methods (as for example, using Gene Clean kit from Biol01) and inserted in a *E.coli*/yeast shuttle vector such as YEP24 (described e.g. by Sanglard D., Kuchler K., Ischer F., Pagani J-L., Monod M. and Bille J., Antimicrobial Agents and Chemotherapy, (1995) Vol.39 No11,

P2378-2386) cut by a restriction enzyme giving compatible ends (for example BamHI for Sau3AI-cut genomic DNA). The resulting expression library can be amplified in *E.coli*. However any known method, appropriate for the preparation
5 of a genomic library, can be used in the present invention.

In order to find the genes in the studied mycete species, which are functionally similar to essential genes of *S.cerevisiae*, one *S.cerevisiae* essential gene is placed under control of a regulated promoter, either as an
10 integrative (1) or extrachromosomal (2) gene.

1. For the integration of a regulated promoter in the *S.cerevisiae* genome, one replaces the native promoter of the selected essential gene by the regulated promoter, for example by homologous recombination via PCR (Güldener
15 et al. (1996)). The homologous recombination via PCR can be carried out for example in the diploid *S.cerevisiae* strain CEN.PK2. The successful integration into one chromosome can be checked in haploid cells following tetrad analysis.

Using the tetrad analysis, one obtains four viable
20 ascospores, wherein in two haploid segregates, the selected essential gene is placed under the control of the native promoter, while the essential gene in the two remaining segregates is placed under the control of the regulated promoter.

25 The last mentioned haploid segregates are used for the transformation with the cDNA or the genomic DNA present in the recombinant vector.

2. Using the extrachromosomal variant, the selected essential *S.cerevisiae* gene is first inserted in a suitable
30 expression vector, for example a *E.coli*/ *S.cerevisiae* shuttle vector. For this purpose, the essential gene may be amplified via PCR from genomic *S.cerevisiae* DNA starting from the ATG initiation codon up to and including the termination codon. The primers used for this purpose may be

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constructed in such a way that they contain recognition sites for appropriate restriction enzymes, facilitating a subsequent insertion under control of a regulated promoter in an expression vector.

5 The recombinant expression vector with the plasmid copy of the essential *S.cerevisiae* gene under the control of a regulated promoter is subsequently used for the transcomplementation of the corresponding mutant allele. The corresponding mutant allele may be selected from the
10 heterozygote-diploid mutant strains prepared by eliminating, partially or totally, by homologous recombination an essential mycete gene listed above and as described above.

 The expression vector with the selected essential
15 *S.cerevisiae* gene is transformed in the corresponding heterozygote-diploid mutant strain carrying instead of the selected essential *S.cerevisiae* gene, a selection marker gene. The transformants are isolated by selection based on the auxotrophic marker contained in the expression vector
20 used. The thus transformed heterozygote-diploid mutant strains are submitted to a tetrad analysis. One obtains four viable segregates. By retracing the corresponding markers of the mutant allele and the expression vector, the transformed wild-type segregates may be distinguished from
25 segregates which do not contain the genomic copy of the essential gene. Segregates, which do not contain the genomic copy of the selected essential gene, are designated as trans-complemented haploid mutant strains. They are subsequently used for transformation with cDNA or genomic
30 DNA libraries from other mycete species present in appropriate vectors.

 As regulated promoters, inducible or repressible promoters may be used. These promoters can consist of naturally and/or artificially disposed promoter sequences.

As regulated promoters, for example the promoters of GAL1 gene and the corresponding promoter derivatives, such as for example promoters, whose different UAS (upstream activation sequence) elements have been eliminated (GALS, 5 GAL1; Mumberg, J. et al. (1994) Nucleic Acids Research 22:5767-5768) may be used. As regulated promoters, promoters of gluconeogenic genes may also be used, such as e.g. FBP1, PCK1, ICL1 or parts therefrom, such as e.g. their activation sequence (UAS1 and/or UAS2) or repression 10 sequence (URS, upstream repression sequence) (Niederacher et al. (1992), Curr. Genet. 22: 636-670; Proft et al. (1995) Mol. Gen. Gent. 246: 367-373; Schüller et al. (1992) EMBO J; 11: 107-114; Guarente et al. (1984) Cell 36: 503-511).

15 A *S.cerevisiae* mutant strain modified in this manner can be cultivated under growth conditions, in which the regulated promoter is active, so that the essential *S.cerevisiae* gene is expressed. The *S.cerevisiae* cells are then transformed with a representative quantity of the 20 library containing the studied mycete species cDNA or genomic DNA. Transformants express additionally the protein whose coding sequence is present in the recombinant vector.

The method contemplates that the growth conditions may be modified in such a way as to inhibit the regulated 25 promoter, under the control of which is the selected essential gene. Especially, growth conditions may be changed by replacing the growth medium. When for example the GAL1 promoter or a derivate thereof is used, one can replace the galactose-containing medium (induced state) by 30 a glucose-containing medium (repressed state).

These modified conditions are lethal for the *S.cerevisiae* cells in which the recombinant vector does not carry the functionally similar genomic DNA or cDNA of the studied mycete species. On the contrary, the *S.cerevisiae*

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cells in which the recombinant vector expresses a functionally similar coding sequence of the studied mycete species, are viable, since in these cells the lethal metabolic defect is complemented by the protein encoded by the functionally similar gene.

The method contemplates that the recombinant vector (the plasmid) is isolated from the surviving transformants using known method (Strathern, J.N. and Higgins, D.R. (1991). Plasmids are recovered from yeast into Escherichia coli shuttle vectors in: Guthrie, C. and Fink, G.R. Methods in Enzymology, Volume 194. Guide to yeast genetic and molecular Biology. Academic Press, San Diego, 319-329) and the cDNA or genomic DNA is analyzed using DNA-analysis methods such as DNA sequencing. (Sanger et al. (1977), Proc. Natl. Acad. Sci. USA 74: 5463-5467)

Essential *S.cerevisiae* genes may thus be used for the identification of functionally similar genes and/or genes homologous in sequence in other mycetes, especially essential genes functionally similar and/or homologous in sequence in mycetes pathogenic to human, animal and plants. For this purpose for example mycetes of the classes phycomycetes or eumycetes may be used, in particular the subclasses basidiomycetes, ascomycetes, especially mehliscomycetales (yeast) and plectascales (mould fungus) and gymnascales (skin and hair fungus) or of the class of hyphomycetes, in particular the subclasses conidiosporales (skin fungus) and thallosporales (budding or gemmiparous fungus), among which particularly the species mucor, rhizopus, coccidioides, paracoccidioides (blastomyces brasiliensis), endomyces (blastomyces), aspergillus, penicilium (scopulariopsis), trichophyton (ctenomyces), epidermophyton, microsporon, piedraia, hormodendron, phialophora, sporotrichon, cryptococcus, candida, geotrichum and trichosporon.

Of particular interest is the use of *Candida* Spp. especially *Candida albicans*, *Candida glabrata*, *Aspergillus* Spp., especially *Aspergillus fumigatus*, *Coccidioides immitis*, *Cryptococcus neoformans*, *Histoplasma capsulatum*,
5 *Blastomyces dermatitidis*, *Paracoccidioides brasiliensis* and *Sporothrix schenckii*.

Starting from the genes of *S.cerevisiae*, identified according to the above-described method, Applicants cloned corresponding essential genes from *C.albicans* i.e. CaOR110,
10 CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, by the following method.

First, oligonucleotide(s) is(are) selected in the sequence of the *S.cerevisiae* gene or a homologous *C. albicans* sequence in order to amplify the corresponding
15 fragment of *C.albicans*. After cloning, the obtained fragment (exhibiting a sequence of about several hundred bp) is used as a probe for screening a *C.albicans* (genomic) DNA library. The screening may include the following steps: clones were spread on dishes, covered with filters
20 where the DNA was crosslinked to the filters, filters are hybridized, the positive colonies are then detected. The selected clone(s) is (are) then sequenced.

The method contemplates that essential mycete genes are used to identify substances which may inhibit partially
25 or totally the functional expression of these essential genes and/or the functional activity of the encoded proteins. Substances may be identified in this fashion, which inhibit mycetes growth and which can be used as antimycotics, for example in the preparation of drugs.

30 The present invention especially covers a method for screening such inhibiting substances, wherein an essential gene from *C.albicans* selected from CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, or a

functionally similar gene in another pathogenic mycete or the corresponding encoded protein is used as target.

By functionally similar genes in other pathogenic mycete species, is meant genes which have a function similar or identical to that of the identified essential genes of *C.albicans*. Functionally similar genes in other pathogenic mycetes may, but need not be homologous in sequence to the corresponding essential *C.albicans* genes. Functionally similar genes in other pathogenic mycetes may exhibit only moderate sequence homology at the nucleotide level to the corresponding essential *C.albicans* genes. By moderate sequence homology it is meant in the present invention genes having a sequence identity, at the nucleotide level, of at least 50%, more preferably of at least 60% and most preferably of at least 70%.

In addition, functionally similar genes in other pathogenic mycetes may, but need not encode proteins homologous in sequence to the proteins encoded by the essential *C.albicans* genes. Functionally similar proteins in other mycetes may exhibit moderate protein sequence homology to the proteins encoded by the essential *C.albicans* genes.

By moderate protein sequence homology is meant in the present invention proteins having a sequence identity, at the amino-acid level, of at least 40%, preferably of at least 50%, more preferably of at least 60% and most preferably of at least 70%.

A particular feature of this method is that essential mycete genes or the corresponding encoded proteins are used as targets for the screening of the substances. The method contemplates that essential *C.albicans* genes as well as functionally similar genes and/or genes homologous in sequence of other pathogenic mycetes or the corresponding encoded proteins may be used as targets.

According to one embodiment of the screening method of the invention, mycetes cells are provided, which contain the essential gene used as target, and those cells are incubated with the substance to be tested. By this way, the growth inhibitory effect of this substance with respect to the essential target gene is determined.

The mycetes cells which express the essential target gene to a different degree are used, and these cells are then incubated with the substance to be tested and the growth inhibitory effect of this substance is determined.

The method includes the use of two or more mycetes cells, or strains derived therefrom, which differ in that they express the essential target gene to a different degree.

For example, two, three, four, five, ten or more mycetes cells or the corresponding mycetes strains may be comparatively analysed with respect to the growth inhibitory effect of a substance used in a defined concentration. Through such expression degree series, antimycotic substances may be distinguished from cytotoxic or inactive substances.

A particular embodiment of the method includes the use of haploid mycetes cells/ strains for the screening, especially haploid *S.cerevisiae* cells/ strains.

The method contemplates the integration of the essential gene selected as a target in a suitable expression vector.

As expression vectors *E.coli*/*S.cerevisiae* shuttle vectors are for example suitable. Especially vectors differing in their copy number per cell may be used. Therefore, one may use vectors, which are present in the transformed *S.cerevisiae* cells in a high copy number, or one can also use those with a low copy number. One embodiment comprises the use of expression vectors which

allow the integration of the target gene in the *S.cerevisiae* genome.

For example the vectors pRS423, pRS424, pRS425, pRS426, pRS313, pRS314, pRS315, pRS316, pRS303, pRS304, pRS305, 5 pRS306 (Sikorki and Hieter, 1989; Christianson et al. 1992) are appropriate as expression vectors.

The vectors of the series pRS423 - pRS426 are present in a high copy number, about 50 - 100 copies/ cell. On the contrary, the vectors of the series pRS313 - pRS316 are 10 present in a low copy number (1 - 2 copies / cell). When expression vectors from these two series are used, then the target gene is present as an extrachromosomal copy. Using the vector of the series pRS303 - pRS306 allows the integration of the target genes into the genome. Using 15 these three different expression vector types allows a gradual expression of the studied functionally similar essential gene.

The method includes that the growth inhibitory effect of substances with respect to mycetes cells/strains is 20 comparatively determined using expression vectors differing for instance in the copy number of the vector/ cell.

Such cells may express the essential target gene to a different degree and may exhibit a graduated reaction with respect to the substance.

25 The method includes also, that a target gene expression of different strength is obtained in different mycetes cells (regulated overexpression) by insertion of the target gene in the expression vector between specific selected *S.cerevisiae* promoters and terminators. 30 *S.cerevisiae* promoters which are constitutively expressed, but with different strength, are suitable. Examples for such promoters are native promoters of *S.cerevisiae* genes MET25, PGK1, TPI1, TDH3, ADH1, URA3, TRP1, as well as corresponding derivatives therefrom, for example promoter

derivatives without specific activator and/or repressor sequences.

Regulated promoters are also appropriate for the graduated over-expression of the target gene. The native
5 promoters of the GAL1 genes and/or corresponding derivatives thereof, for example promoters, in which different UAS elements have been eliminated. (GALS, GALL; Mumberg et al. (1994) Nucleic Acids Research 22: 5767-5768) as well as promoters of gluconeogenic genes, for example the promoters
10 FBPI, PCK1, ICL1, or parts thereof, for example their activator- (UAS1 or UAS2) or repressor- (URS) sequences are used in corresponding non activable and/or non repressible test promoters (Schüller et al. (1992) EMBO J. 11: 107-114) Guarente et al. (1984) Cell 36: 503-511; Niederacher et al.
15 (1992) Curr. Genet. 22: 363-370; Proft et al. (1995) Mol. Gen. Genet. 246: 367-373).

In the expression vector terminator for example the terminator sequence of *S.cerevisiae* genes MET25, PGK1, TPI1, TDH3, ADHI, URA3 may be used.

20 The method includes that by the use of cleverly selected expression vector types and/or the preparation of suitable expression vectors, eventually using promoters of different strength and differently regulated promoters, a series of expression vectors may be constructed, all
25 containing the same target gene, but differing in that they express the target gene to a different extent.

The method includes the transformation of the expression vector in haploid wild-type cells of *S.cerevisiae*. The thus obtained *S.cerevisiae* cells/strains
30 are cultivated in liquid medium and incubated in the presence of different concentrations of the tested substance and the effect of this substance on the growth behaviour of the cells/strains expressing the target gene to a different degree is comparatively analysed. The method

also includes that haploid *S.cerevisiae* cells/strains, transformed using the respective expression vector type without target gene, are used as a reference.

The method includes that the screening of the
5 substances can be carried out in different media using regulated promoters, especially GAL1 promoter and its derivatives (GALS and GALL), since the expression degree may be largely influenced by the choice of the respective medium. Thus, the expression degree of the GAL1 promoter
10 decreases in the following fashion: 2 % galactose > 1 % galactose + 1 % glucose > 2 % glycerine > 2 % glucose.

The effect of the substances inhibiting the growth of wild-type cells of *S.cerevisiae*, may be partially or totally compensated by the overexpression of the
15 functionally similar gene of another mycete species.

According to one embodiment, the method for screening antimycotic substances is carried out in vitro by contact of an essential or functionally similar gene or the corresponding encoded protein with the substance to be
20 tested and determination of the effect of the substance on the target. Any in vitro test appropriate for determining the interaction of two molecules, such as a hybridization test or a functional test, can be used (e.g. enzymatic tests which are described in details in Bergmeyer H.U.,
25 Methods of Enzymatic Analysis, VCH Publishers). If the screening is carried out using the encoded protein as the target, then the corresponding essential gene is inserted by any suitable method known in the art, such as PCR amplification using a set of primers containing appropriate
30 restriction sites, (Current Protocol in Molecular Biology, John Wiley and Sons, Inc) into an expression system, such as *E. coli*, Baculovirus, or yeast, and the expressed protein is then completely or partially purified by a method known in the art. Any purification method

appropriate for the purification of expressed proteins, such as affinity chromatography can be used. If the target protein function is known, a functional test can then be carried out in which the effect of the antimycotic substance on the protein function is determined. If the protein function is unknown, substances which can interact with the target protein, e.g. which bind to the encoded protein, can be tested. In such a case a test such as protection of the target protein from enzymatic digestion by appropriate enzymes can be used.

According to one specific embodiment, the method for screening antimycotic substances corresponds to an enzymatic assay wherein the activity of dihydropneopterin aldolase (DHNA) and/or dihydropteroate synthase (DHPS) and/or 7,8-dihydro-6-hydroxymethylpterin-pyrophosphokinase (HPPK) is determined; the enzymatic assay can be such as disclosed in "Bergmeyer H.U., Methods in Enzymatic analysis, VCH Publishers".

Dihydropneopterin aldolase (DHNA) catalyses the conversion of 7,8-dihydroneopterin into 6-hydroxymethyl-7,8-dihydropterin (with emission of CH_2OHCHO). Dihydropteroate synthetase (DHPS) catalyses the condensation of 6-hydroxymethyl-7,8-dihydropterin pyrophosphate to para-aminobenzoic acid to form 7,8-dihydropteroate which corresponds to the second step in the three-step pathway leading from 6-hydroxymethyl-7,8-dihydropterin to 7,8-dihydrofolate. 7,8-dihydro-6-hydroxymethylpterin-pyrophosphokinase (HPPK) catalyzes the attachment of pyrophosphate to 6-hydroxymethyl-7,8-dihydropterin to form 6-hydroxymethyl-7,8-dihydropterin pyrophosphate which corresponds to the first step in a three-step pathway leading to 7,8-dihydrofolate. All organisms require reduced folate cofactors for the synthesis of a variety of metabolites. Most microorganisms must synthesize folate de novo because they lack the active transport system of higher vertebrate cells which allows these organisms to use dietary folates. Enzymes involved in folate biosynthesis are therefore targets for a variety

of antimicrobial agents. Consequently, these enzyme activities are essential to the microorganisms, and are absent in man.

The method also includes the identification of genes
5 which are functionally similar and/or homologous in sequence to essential *C.albicans* genes from humans, animals or plants. The corresponding human, animal or plant genes may optionally be used as target genes in the method in order to test if antimycotic substances exhibit an effect
10 on these target genes.

A particular advantage of the method is that in this way substances may be identified which efficiently inhibit mycetes growth and also the influence of these substances on corresponding functionally similar genes and/or genes
15 homologous in sequence to essential *C.albicans* genes from human, animal or plants may be determined.

The method includes also the possibility to check the existence of functionally similar genes and/or human, animal or plant genes homologous in sequence to the
20 corresponding essential mycete genes, for example by checking homology of the identified essential mycete genes or parts thereof with human, animal or plant sequence genes available in data banks. In this way, it is possible to select at an early stage from the identified essential
25 mycete genes, depending on the aim, those for which no functionally similar gene and/or no human gene homologous in sequence exist, for example.

Thereby, the method offers a plurality of possibilities to identify selectively substances with
30 antimycotic effects, with no harmful effect on human beings.

For example, it is possible to identify substances usable for the preparation of drugs for the treatment of mycosis or prophylaxis in immunodepression states. These

substances may be used for example for the manufacture of drugs usable for the treatment of mycotic infections, which occur during diseases like AIDS or Diabetes. Substances which may be used for the fabrication of fungicides, especially of fungicides which are harmless for humans and animals, can also be identified.

Furthermore, the method offers the possibility to identify antimycotic substances, which selectively inhibit growth of specific mycete species only.

The screening method is particularly advantageous inasmuch as it is sufficient to know whether the genes are essential, one does not need any additional information regarding the function of the essential genes or the function of the encoded proteins. In addition, it is particularly advantageous for the identification of functionally similar genes to essential *S.cerevisiae* gene, in other mycetes where the DNA sequence is not available for many of these genes.

According to another aspect the invention provides an antibody directed against the protein encoded by the CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, gene or a polypeptidic fragment thereof. The term "antibody" encompasses monoclonal and polyclonal antibodies. Said antibodies can be prepared by method well known in the art such as those disclosed in "Antibodies, a laboratory manual", Ed. Harbow and David Lane. Cold Spring Harbor Laboratory Eds., 1988.

According to another aspect the present invention provides a kit for the diagnosis of fungal infections comprising a gene selected from the group consisting of CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 and CaJL039, a functionally similar gene thereof, a functional fragment thereof, the corresponding encoded protein, a functional polypeptide fragment thereof or an antibody

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directed against the protein encoded by CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039 gene or by a functionally similar gene, or a polypeptidic fragment thereof. Such kits can be prepared using any suitable method well known in the art.

Examples

Example 1 : CaNL256

The Internet site of Stanford (<http://candida.stanford.edu/>) gives access to preliminary sequences of the genome of *C. albicans*. One of these sequences has homology with the YNL256 gene of *S. cerevisiae*. Two oligonucleotides were selected in this sequence (5'-ATTCATCCCATCAGTGCAGAAAG-3' and 5'-ATTGACCAATAGCTCTAATTAATG-3') in order to amplify the corresponding fragment of *C. albicans*. After cloning, we obtained a sequence of 399 bp close to the expected sequence (SEQ ID NO:1). The deduced protein was compared with the one of YNL256, evidencing 53% similarity and 43% identity (fig.1). This fragment of 399 bp of *C. albicans* was used as a probe for screening a genomic library of *C. albicans*. The latter was prepared by partial digestion of genomic DNA of *C. albicans* by Sau3AI and cloning into the YEP24 vector at the BamHI site. The clones of the library were then spread at a density of 2000 clones per dish. Each dish was covered by a nitrocellulose filter which was then successively treated with: NaOH, 0.5M, 5 minutes; Tris, 1M, pH 7.7, 5 minutes; Tris, 0.5M, pH 7.7, NaCl, 1.25M, 5 minutes. After drying, the filters were kept for 2 hours at 80°C. Prehybridization and hybridization were carried out in a buffer of 40% formamide, 5xSSC, 20 mM Tris pH 7.7 1xDenhardt 0.1% SDS. The probe was labeled with 32P with the RediPrime kit and dCTP from Amersham UK. Hybridization took place over 17 hours at 42°C. The filters were then washed in 1x SSC, 0.1% SDS, three times

for 5 minutes at room temperature and then twice for 30 minutes at 60°C, and were then submitted to autoradiography overnight. The colonies corresponding to the spots obtained were reisolated by re-spreading at low density followed by further hybridization. Three clones were thus obtained (out of 40,000), which were sequenced on an ABI 377 apparatus. The sequences were compiled using the ABI software and then analysed using the GCG software package. One of these three clones turned out to contain the complete coding sequence corresponding to the probe used; this gene was called CaNL256, whose sequence is represented in SEQ ID NO:2. CaNL256 has 52% of nucleotides identical to YNL256 of *S. cerevisiae*. The coding region is shorter at the N-terminus. For translation to amino acids, account was taken of the fact that, in *C. albicans*, the CTG codon is translated to Serine (there are 3 CTG codons in CaNL256). The deduced protein had 40% amino acids identical with YNL256 of *S. cerevisiae* and 41% with FAS (folic acid synthase) of *Pneumocystis carinii*. Investigation into the databases using the Blast software showed homology of two parts of the CaNL256 protein with, respectively, the bacterial enzymes Dihydropteroate Synthase (EC 2.5.1.15) (DHPS) of *Haemophilus influenzae*, *Staphylococcus haemolyticus*, *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Bacillus subtilis*, *Clostridium acetobutylicum*, *Escherichia coli*, *Mycobacterium leprae* (P value less than e^{-28}) and 7,8-dihydro-6-hydroxymethylpterin-pyrophosphokinase (EC 2.7.6.3) (HPPK) of *Bacillus subtilis*, *Escherichia coli*, *Haemophilus influenzae*, *Streptococcus pneumoniae* (P value less than e^{-20}). The units characteristic of DHPS and HPPK are also found in CaNL256.

Example 2 : CaBR102

The Internet site of Stanford (<http://candida.stanford.edu/>) give access to preliminary sequences of the genome of *C. albicans*. One of these sequences has homology with the YBR102 gene of *S.cerevisiae*. Two oligonucleotides were selected in this sequence (5'-AGTATTCAATTGGGTATTCC-3' and 5'-CCGGCATCATCAGTAACTCC-3') in order to amplified the corresponding fragment of *C. albicans*. After cloning, we obtained a sequence of 647 bp (SEQ ID NO:3). The deduced protein was compared with the one of YNL102, evidencing 35% similarity and 26% identity (fig.2). This fragment was amplified using Pfu polymerase (Stratagene). The PCR product was purified (High Pure PCR Product Purification Kit, Boehringer Mannheim) and used as a probe for screening a *C. albicans* genomic DNA library. The latter was prepared by partial digestion of *C. albicans* genomic DNA with SauIIIA and cloning into the YEP-24Trp1 vector at the BamHI restriction site. 40,000 clones of the library were then spread at a density of 2000 clones per dish. Each dish was covered by a nitrocellulose filter (Membrane Hybond N⁺, Amersham) which was then successively treated with : 1.5 M NaCl/0.5 M NaOH, 5 minutes; 1.5 M NaCl/0.5 M Tris-HCl pH 7.2/1 mM EDTA, 3 minutes, twice; DNA was crosslinked to the filters (Amersham Life Science, ultra violet crosslinker). The probe (100 ng) was labelled with ³²P using the RediPrime kit and dCTP (Amersham Life Science). The filters were hybridized in a buffer containing 30% formamide, 5 x SSC, 5% Denhart's solution, 1% SDS, 100 µg /ml salmon sperm DNA and a probe concentration of 10⁶ cpm/ml at 42°C for 16 h. The membranes were then washed three times at room temperature in 2 x SSC/0.1% SDS for 5 minutes each and three times in 1 x SSC/0.1% SDS at 60°C for 20 minutes each. the filters were then exposed overnight to an X-ray

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film. The colonies corresponding to the positives clones were isolated and screened a second time by the same procedure. Two positives clones were finally obtained, which were sequenced on an ABI377 apparatus. the sequences
5 were compiled using ABI software and then analysed using the GCG software package. The nucleotide sequences of these two clones were identical and contained the complete coding sequence corresponding to the probe used, this gene was called CaBR102, whose sequence is represented in SEQ ID
10 No:4. The translation of this nucleotide sequence was examined, account was taken of the fact that in *C. albicans* the CTG codon is translated to serine (there are 3 CTG codons in CaBR102). The deduced protein has 24% identity to *S. cerevisiae* gene YBR102.

15 Example 3 : CaIR012

Chromosomal DNA from the *C. albicans* strain Caf2-1 was isolated using Yeast Cell Lysis prep Kit and Genome DNA Kit from BIO101. A 343 bp fragment from *C. albicans* genomic DNA (SEQ ID NO:5) was amplified with the oligonucleotide
20 primers CaYIR012-5' (5'-GACGTCGTAGACGATACTCAAGAAG-3') and CaYIR012-3' (5'-CTGCAGTAAACCCTCCAGATATAACAG-3') by PowerScript DNA polymerase (PAN Systems GmbH) using the hot start technique. The PCR product was purified from the agarose gel and labeled with fluorescein (Gene image random
25 prime labelling module, Amersham Life Science) according to the manufacturer's instructions. Plasmid DNA from *E.coli* was isolated using Qiagen columns as recommended by the manufacturer. Screening the λ ZAPII *C. albicans* cDNA library was performed following the manufacturer's
30 instructions (Stratagene Ltd.). Nylon filters (Schleicher&Schuell) were lifted from LB-plates (150 mm) with 15000 pfu/plate, denatured 5 min in 1.5M NaCl, 0.5M NaOH, neutralized 3 min in 1.5M NaCl, 0.5M Tris-HCl pH8.0, washed 3 min in 0.2 M Tris-HCl pH 7.5, 2xSSC and DNA was

crosslinked to the filters (Stratagene UV crosslinker). The filters were prehybridized 4 h at 60 °C and hybridized with the fluorescein-labeled DNA probe overnight at 60 °C. Detection was performed with Anti-fluorescein AP conjugate (Signal amplification module for the FluorImager, Amersham LIFE SCIENCE) and analysed after 20 h with a Fluorimager (Storm 860, Molecular Dynamics). Positive plaques were picked and incubated with 0.5 ml SM-buffer (100mM NaCl, 8 mM MgSO₄, 50 mM Tris-HCl pH7.5, 0,01% gelatin). The selected clones were diluted, titered with host cells XL1-Blue and screened and purified a second time by the same procedure. Finally, the pBluescript SK(-) phagemid containing the DNA insert of interest was rescued by the ExAssist Helper Phage system according to the Stratagene protocol. From a total of 75000 screened plaques, 3 positive clones were identified. pBluescript SK (-) phagemid DNA was isolated, sequenced with T3 and T7 primers and the sequences were extended with custom-synthesized oligonucleotide primers. Nucleotide sequence analyses were performed with the Gene Data software package (Gene Data AG, Basel Switzerland). Similarity searches with the Swissprot database were conducted with the BLAST program (Gish, Warren and David J. States (1993). Identification of protein coding regions by database similarity search. Nat. Genet. 3:266-72.). One of these three clones turned out to contain the complete coding sequence corresponding to the probe used; this gene was called CaIR1012, whose sequence is represented in SEQ ID NO:6.

Example 4: CaJL039

The CaJL039 sequence is depicted in SEQ ID No 7.

The CaJL039 gene was cloned based on gene fragment data issued from the public Stanford *Candida albicans* sequencing database.

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(a) A fragment that showed homology to *Saccharomyces cerevisiae* YJL039c was identified, the sequence of which is given in SEQ ID No 8.

Using the procedure disclosed in example 3 with the
 5 oligonucleotide primer pair (Ca039s: TAG CTC AAC CTA CCA
 CCA ATC /Ca039r: ATC ACA AGA CTG TCA ATG TAA AT), a short
 PCR fragment (234 base pairs long) was amplified for
 screening a *Candida albicans* cDNA lambda ZAP II library
 (gift of Alistair Brown, Aberdeen).

10 Three positive clones of the 3' coding region were
 obtained. (# 21t7, 11t3, 21t3).

(b) 3'- and 5'- extension of the internal
 fragment using the primer walking method

The Sanglard genomic *Candida* DNA library with the
 15 YEp24 vector backbone was used for further amplification of
 3'- and 5'-coding sequences. Amplification was carried out
 by using the following vector-specific oligonucleotide
 primers and CaJL039 fragment-specific primers:

cggaattcctatcgactacgcatcatgg: YEp24for (vector
 20 specific)
 gcgaattccgatataggcgccagcaac: YEp24ba (vector
 specific)
 caattgctttgactcgggtgttattaagt: Ca039-51 (CaJL039:
 5'fishing)
 25 tcttggcacaacttgataagaatctgt: Ca039-52 (~)
 taggtgtacgcgaaagccaagtagaac: Ca039-53 (~)
 ttgttaatcgtacacctaaggtgttgac: Ca039-31 (CaJL039:
 3'fishing)
 ttgcagattgatgctagcaatgtatttg: Ca039-32 (~)
 30 Using the technique of primer walking, the complete
 5'-sequence could be amplified (clone 14b-1-1 and clone
 17b-3-4).

The missing 3'-sequence was available from GTC
 PathoGenome Release 5.0, contig #2830.

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An interacting protein (C82, component for RNA polymerase III in yeast) has been identified.

Example 5: CaOR110

5.1. CaOR110

5 The CaOR110 sequence is depicted in SEQ ID No 9.

CaOR110 was cloned based on gene fragment data issued from the public Stanford *Candida albicans* sequencing database.

(a) A small ScOR110-homologous fragment was used in a hybridization experiment to identify CaOR110 clones in a *Candida Albicans* lambda ZAPII cDNA library (from Alistair Brown). Alignment of *Candida Albicans* CaOR110 sequence with the fragment used for hybridization is given in figure 3. The homologous fragment sequence is given in SEQ ID No. 15 17.

(b) 3'- and 5'- Extension of the internal fragment:

The Sanglard genomic *Candida* DNA library (received from RMV) in the YEP24 vector backbone was used for the amplification of 3'- and 5'- coding and non-coding sequences. This amplification was done by using the vector-specific oligos (directional towards the insert) and CaOR110 fragment-specific oligos (directional towards the vector flanking sequences) described below:

cggaattcctatcgactacgcatcatgg : YEP24for
 25 gcgaattccgatataggcgccagcaac : YEP24ba
 cgggatccggttaaccaattggatctataaccgtg : 110-ba-150
 gcggatcctggtgcccttggtggtgaatg : CaYOR110A
 gcggatccctcacaatatgacgattgaaact : CaYOR110B
 ggcgtcgactcaggcgccagttttacgtacttcaaattcatc : CaYOR110C
 30 tgtgaattcttgacacagggtga : CaYOR110D
 caaaccttcagcacaaactcca : CaYOR110E.

The finally assembled sequence that included also 3'- and 5'- non-coding sequences was verified by sequencing. The coding region was subcloned into the p414RSGALL-vector.

The map is depicted in Fig. 4.

The homologous yeast ORF (YOR110w) has been described as the transcription factor subunit TFC7 interacting with TFC1 in the TFIIIC polymerase complex (Manaud et al., 1998, Mol. Cell. Biol. 18; 3191-3200).

5.2. CaOR110 splice variant

For CaOR110, an additional splice variant was identified. The clones for the splice variant of CaOR110 were obtained from a *Candida albicans* cDNA library.

10 The sequence is depicted in SEQ ID No.10.

The splice variant uses the donor site "gtacgt" at position 907 of the original CaOR110 sequence. Acceptor site is at 1047. The map is disclosed in Fig. 5.

15 The alignment of the original CaOR110 and the splice variant is given in fig. 6.

Example 6 : CaMR212

The CaMR212 sequence is depicted in SEQ ID No. 11.

(a) CaMR212 was cloned based on gene fragment data from the public Stanford *Candida albicans* sequencing database.

20 The sequence of a fragment showing homology (Blast search) to the *Saccharomyces cerevisiae* gene YMR212c is given in SEQ ID 12.

25 Based on these data, the following oligos were designed that allow amplification of this fragment (490 bp-fragment) from genomic *Candida albicans* DNA.

Oligos:

CaYMR212for: 5'- cacctgtgaacaacccaccatc-3'

CaYMR212back: 5'- gaatatacctttttaactcaagag -3'

30 (b) 3'- and 5'- extension of this internal fragment from CaMR212

For this purpose, genomic *Candida* DNA libraries from Dominique Sanglard (received from RMV) were used. The YEp24 backbone of this library was used to amplify the 3'- and 5'- coding and non coding sequences with PCR. This was done

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by using oligos specific for the CaMR212 490 bp-fragment (directional towards the vector flanking regions) and vector-specific oligos (directional towards the insert).

Oligos:

5 YEP24for (vector specific):

5'-cggaattcctatcgactacgcgatcatgg

YEP24ba (vector specific):

5'-gcgaattccgatataggcgccagcaac

Primer YEp24for and CaMR212for gave a 500 bp fragment,
10 encoding 5'-UTR and the 5'coding region from CaMR212.

Using primer YEp24 for and CaMR212back a 1400 bp CaMR212-fragment was amplified. Using the sequence of this 1400 bp-fragment the following new primers, specific for this fragment were designed.

15 Oligos:

Ca212-1: 5'- gctttcccagcaggataacattg

Ca212-2: 5'- tgagttataatgcagctgttgg

Ca212-3: 5'- catctcgtgtgaacatgattgg

Primers YEP24 for and Ca212-3 gave a 1600 bp fragment,
20 coding for the 3'- coding region and the 3'UTS region.

With the 3 PCR fragments the 2900 bp sequence (including coding and 3'and 5'-non-coding sequences) was assembled. With the following new primers the coding sequences was amplified from genomic DNA and cloned into
25 p413GALL-vector.

Oligos for amplifying coding region:

Ca212for: 5'- agtttcttcaacttccagatccaag

Ca212back: 5'- gatatattgcaactgtctctctctc

The yeast homolog YMR212c plays a role in cell wall
30 function because the knockout can be rescued in 1M sorbitol. In addition, YMR212c under GAL-promoter regulation shows an increased sensitivity versus Congo Red and Calcofluor White. YMR212c is an integral membrane protein and localizes to the plasma membrane (demonstrated

by microscope analysis of YMR212-GFP fusion proteins and by biochemical analysis of YMR212-GST fusion proteins).

Example 7 : CaDR325

The CaDR325 sequence is given at SEQ ID 13.

5 CaDR325 was cloned based on gene fragment data from the public Stanford *Candida albicans* sequencing database.

(a) 3 fragments that showed homology to *Saccharomyces cerevisiae* YDR325 were identified, the sequences of which are disclosed in SEQ ID 14, 15 and 16.

10 Based on these data, the following oligos were designed that allowed the verification of the database sequences and the amplification of an approx. 2200 bp internal CaDR325 fragment from genomic DNA:

cgagcatctacttggttcaaccac: hybCaYDR325ba Oligo
 15 gaatctctggctcgctc: 325-juls Oligo
 gaccgagatacagagaat: 325-julr Oligo
 ggtaaatagatcgtgatgaat: Ca325r Oligo
 caacctcactgacaaataactt: Ca325s Oligo

The finally subcloned 2200 bp internal fragment was
 20 amplified by the combination hybCaYDR325ba + 325-julr oligos.

(c) 3'- and 5'- Extension of the internal fragment:

The Sanglard genomic *Candida* DNA library (received from RMV) in the YEP24 vector backbone was used for the
 25 amplification of 3'- and 5'- coding and non-coding sequences. This was done by using the following vector-specific oligos (directional towards the insert) and CaDR325 2200 bp fragment-specific oligos (directional towards the vector flanking sequences):

30 cggaattcctatcgactacgcgatcatgg : YEP24for (vector specific)
 gcgaattccgatataggcgccagcaac : YEP24ba (vector specific)
 acgcttccaatgtattattctcg : Oligo 1-10-A back

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	ggatgccaaatttcctga :	Oligo 1-10-B for
	catccagaagatataacggct :	Oligo 1-10-C for
	tgcataatctaattcagcgaca :	Oligo 1-10-D back
	gtggttgaacaagtagatgctcg :	Oligo 1-10-E for
5	gcgcttgaaaccactagtgattg :	Ca325Klon_2_Fo
	caattcactagtggtttcaagcgc :	Ca325Klon_3_Ba

The finally assembled 4700 bp sequence that included also 3'- and 5'- non-coding sequences were verified by sequencing. The coding region was subcloned into the
10 p413RSGALL-vector.

The map is disclosed in fig. 7.

Sequences numbers are identified in field 130 of the sequence listing.

Claims:

1. A polynucleotide having the sequence as depicted in the sequence selected from the group consisting of SEQ ID No.2, SEQ ID No.4, SEQ ID No.6, SEQ ID No.7, SEQ ID No.9, SEQ ID No.10, SEQ ID No.11 or SEQ ID No.13, homologs thereof and functional fragments thereof.

2.-The polynucleotide of claim 1 which is the gene CaNL256, homologs thereof and functional fragments thereof.

3.-The polynucleotide of claim 1 which is the gene CaBR102, homologs thereof and functional fragments thereof.

4.-The polynucleotide of claim 1 which is the gene CaIR012, homologs thereof and functional fragments thereof.

5.-The polynucleotide of claim 1 which is the gene CaMR212, homologs thereof and functional fragments thereof.

6.-The polynucleotide of claim 1 which is the gene CaDR325, homologs thereof and functional fragments thereof.

7.-The polynucleotide of claim 1 which is the gene CaOR110, homologs thereof and functional fragments thereof.

8.-The polynucleotide of claim 1 which is the gene CaJL039, homologs thereof and functional fragments thereof.

9 -A protein encoded by the polynucleotide according to claim 2 or a functional polypeptide fragment thereof.

10 -A protein encoded by the polynucleotide according to claim 3 or a functional polypeptide fragment thereof..

11 -A protein encoded by the polynucleotide according
to claim 4 or a functional polypeptide fragment thereof.

12 -A protein encoded by the polynucleotide according
5 to claim 5 or a functional polypeptide fragment thereof.

13 -A protein encoded by the polynucleotide according
to claim 6 or a functional polypeptide fragment thereof.

10 14 -A protein encoded by the polynucleotide according
to claim 7 or a functional polypeptide fragment thereof.

15 15 -A protein encoded by the polynucleotide according
to claim 8 or a functional polypeptide fragment thereof.

16.-A plasmid deposited at the CNCM with the accession
number I-2065.

17.-A plasmid deposited at the CNCM with the accession
20 number I-2063.

18.-A plasmid deposited at the DSMZ with the accession
number DSM 12977.

25 19.-A plasmid deposited at the DSMZ with the accession
number DSM 12976.

20.-A plasmid deposited at the DSMZ with the accession
number DSM 12978.

30 21.-A plasmid deposited at the DSMZ with the accession
number DSM 12979.

22.- An antibody directed against the protein of claim
35 9 or a functional polypeptide fragment thereof.

23.- An antibody directed against the protein of claim
10 or a functional polypeptide fragment thereof.

24.- An antibody directed against the protein of claim
5 11 or a functional polypeptide fragment thereof.

25.- An antibody directed against the protein of claim
12 or a functional polypeptide fragment thereof.

10 26.- An antibody directed against the protein of claim
13 or a functional polypeptide fragment thereof.

27.- An antibody directed against the protein of claim
14 or a functional polypeptide fragment thereof.
15

28.- An antibody directed against the protein of claim
15 or a functional polypeptide fragment thereof.

29.-A polynucleotide obtainable by the process
20 comprising the following steps:

(i) selecting an essential gene from
Saccharomyces cerevisiae;

(ii) comparing the sequence of said gene with
Candida Albicans genome sequences;

25 (iii) deducing homologous oligonucleotides
regions;

(iv) PCR amplifying the thus-obtained
oligonucleotides;

(v) using the amplimers of step (iv) for
30 detecting the complete gene of interest;

and homologs thereof and functional fragments thereof.

30.-The polynucleotide of claim 29, in which step (v)
is comprised of the step of using the amplimers of step
35 (iv) as a probe for detecting the complete gene of interest
from a Candida albicans genomic library.

31.-The polynucleotide of claim 29, in which step (v) is comprised of the step of using the amplimers of step (iv) as a probe for detecting the complete gene of interest from a *Candida albicans* cDNA library.

32.-The polynucleotide of claim 29, in which step (v) is comprised of the step of 3' and 5' extension of the amplimer using a PCR method.

33.-A method for the screening of antimycotic substances wherein an essential gene from mycetes or a functionally similar gene from another pathogenic mycete, or the corresponding encoded protein, is used as target and wherein the essential gene is selected from the group consisting of CaNL256, CaBR102, CaIR012, CaMR212, CaDR325, CaOR110, CaJL039, homologs thereof and functional fragments thereof.

34.-The method of claim 33 wherein mycete cells which express the essential gene, or a functionally similar mycete gene, to a different level are incubated with the substance to be tested and the growth inhibiting effect of the substance is determined.

35.-The method of claim 33 wherein said target gene or the corresponding target encoded protein is contacted in vitro with the substance to be tested and the effect of the substance on the target is determined.

36.-The method according to claim 33 wherein the screened substances partially or totally inhibit the functional expression of the essential genes or the functional activity of the encoded proteins.

37.-The method according to claim 33 wherein the screened substances partially or totally inhibit the activity of dihydropneopterin aldolase (DHNA).

5 38.-The method according to claim 33 wherein the screened substances partially or totally inhibit the activity of dihydropteroate synthase (DHPS).

10 39.-The method according to claim 33 wherein the screened substances partially or totally inhibit the activity of 7,8-dihydro-6-hydroxymethylpterin-pyrophosphokinase (HPPK).

15 40.-The method according to claim 33 wherein the mycete species are selected from the group comprising Basidiomycetes, Ascomycetes and Hyphomycetes.

20 41.- The method according to claim 33, wherein said functionally similar genes are essential genes from Candida Spp, or Aspergillus Spp.

25 42.- The method according to claim 41, wherein said functionally similar genes are essential genes from Candida albicans, or Aspergillus fumigatus.

30 43.- A kit for diagnosis of fungal infections comprising a gene selected from the group consisting of CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 and CaJL039, a functionally similar gene thereof, a functional fragment thereof, the corresponding encoded protein or a functional polypeptidic fragment thereof, or an antibody directed against the protein encoded by the gene selected from the group consisting of CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 and CaJL039, or by a functionally similar gene, or a polypeptidic fragment thereof.

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USING SAID GENES

(57) Abstract: The present invention concerns essential genes from C. albicans and their use in a method for the screening of an-
timycotic substances.

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Fig.1

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1 .....IHPISAESLHSHLQQLINDKPQ 22
      :||:| | : ||| | . .
451 PDLNIPHPRMLERTFVLEPLCELISPVHLHPVTAEPIVDHLKQLYDKQHD 500

23 ETV.....QESSDLLQFIPVSRLPVKDNILKFDQINHKSPTLIMGIL 64
      |         | .|:         |         ||| || |
501 EDTLWKLVPLPYRSGVEPRFLKFKTATKLDEFTGETNRITVSPTYIMAIF 550

65 NMTPDSFSDGGKHFG...KELDNIVKQA.EKLVSEGATIIDIGGVSTRPG 110
      | ||||| |||.|| :|..|:| : | . |||:| ||||
551 NATPDSFSDGGEHFADIESQLNDIIKLCKDALYLHESVIIDVGGCSTRPN 600

111 SVEPTEEEEELERVIPLIRAIQS..... 133
      |:: .|||: | |||:||||:|
601 SIQASEEEEIIRRSIPLIKAIRESTELPQDKVILSIDTYRSNVAKEAIKVG 650
```


Fig. 2

```

251 NDLNEVLDDQCTKIAEKRLQLQDQIDQERQGNFNNVESHSNSPALLPLKA 300
      1 .....KSIQL 5
301 GQNGNLMRRDRSSVLILEKFWDTELDQLFKNVEGAOKFINSTKGRHILMN 350
      | | :|||::|. | ||:| |||.:|| ||: |||.  |||.
      6 GIPSN.KKKDRSSIMVLKKMWDSQLQSLFKHVDGASKFVQPLPNRHIVAE 54
351 SANWMELNNTTGTGKPLQMVQIFILNDLVLIADK...SRDKQNDFIVSQYCP 397
      | | |. | || :|| |||:||| | | |. :. |
      55 SGRWFEVNVGNWVKPSYPHTLFIENDLILIAVKKSSSSSQEPTTGGSNNGS 104
398 LKDVTVTQEEFSTKRLLFKFSNSNSSLYECDRADECSRLLDVI..RKAKD 445
      | | |. | |. | |. | |. | |. | |. | |. | |.
      105 KSRLQAVQCWPLTQVSLQQIKSPKKDDDKMYFINLKSLSYVYLTDRYD 154
446 DLCDIFHVEEENSKRIRESFRYLQSTQQTGRENRRSPNKNK..RRSMGG 493
      : : :||| | | |. | | | |. : | | : | | :
      155 HFVKVTEAFNKGKNEMIQSERLLDSRLSSPSNNGGDSKEEKRLRESLRN 204
494 SITPGRNVTGAMDQYLLQNLTLSMHSRPRSRDMSSTAQRLKFLDEGVEEI 543
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      205 SGNYKEGVTTDAGGAATG*VT..... 225

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FIG. 3

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421 CGATAAATTATTGATCGATGAAGATACTTGGCCAAGAGATAACTTAAATGTTATACCTAA
    0 -----
481 TATTGAAGGAGAAGATTATGATGAAATCTACGATCGTGCCAAATTGTTTTGGAAAAAGTT
    0 -----
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                                     ||||| |||||||||||||||||||
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      601 AGCAACGAAAAATTGCTTTAGGATCAGCTTTATTACAGTTAAAAATCAGTTACTGATGTTAT
          89 AGATGATAATCAAACGTGTGTTACGTGCTGGTGCATGTTTCATTATCCAAATTGTTAGAGA
            ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| |||||||
           661 AGATGATAATCAAACGTGTGTTACGTGCTGGTGCATGTTTCATTATCCAAATTGTTAGAGA
               149 TGGCGAAGATAAAAACCAATCATACTATTCAATGGAAAATTGTCATGAATGGTAATTGTGA
                 ||||||| ||||||| ||||||| ||||||| ||||||| ||||||| |||||||
                721 TGGCGAAGATAAAAACCAATGATACTATTCAATGGAAAATTGTCATGAATGGTAATTGTGA
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                   781 ATTCTTGACACAGGGTGAAGAAATGAACTGGGATTTCGTCGTGGTGTGTAAGCCGGGTC

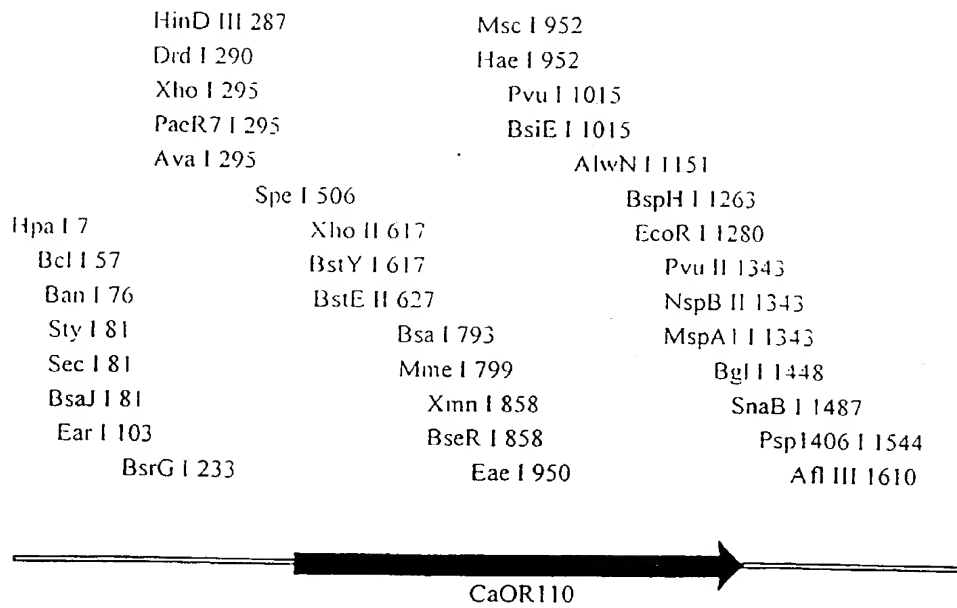
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FIG. 4



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FIG. 5

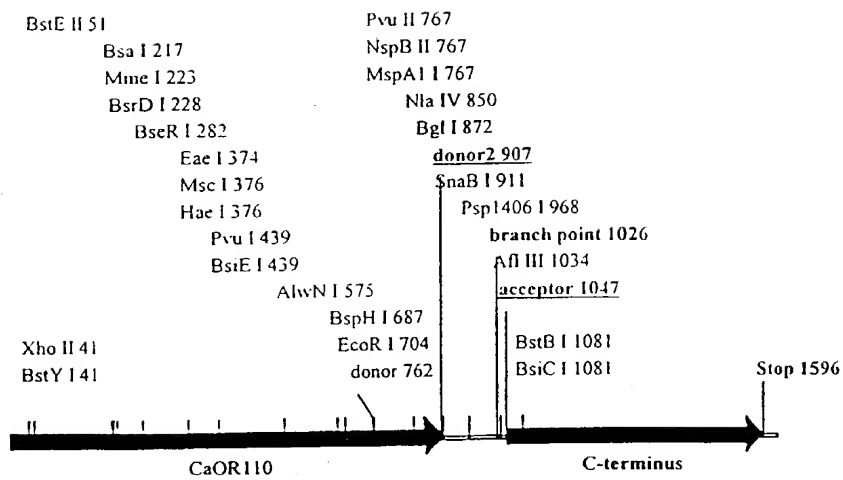


FIG. 6

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121	GAACAAGCCCAACAGTTAGCTGCCTATCTTACATCATTACCTACACATGAAAAGCCTGAA	180
121	GAACAAGCCCAACAGTTAGCTGCCTATCTTACATCATTACCTACACATGAAAAGCCTGAA	180
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1361 CTATCATGGATATAGATCAAGACTCACAAAGGACAACAACAGCTAGAAGTCAGTTCTTAA 1420
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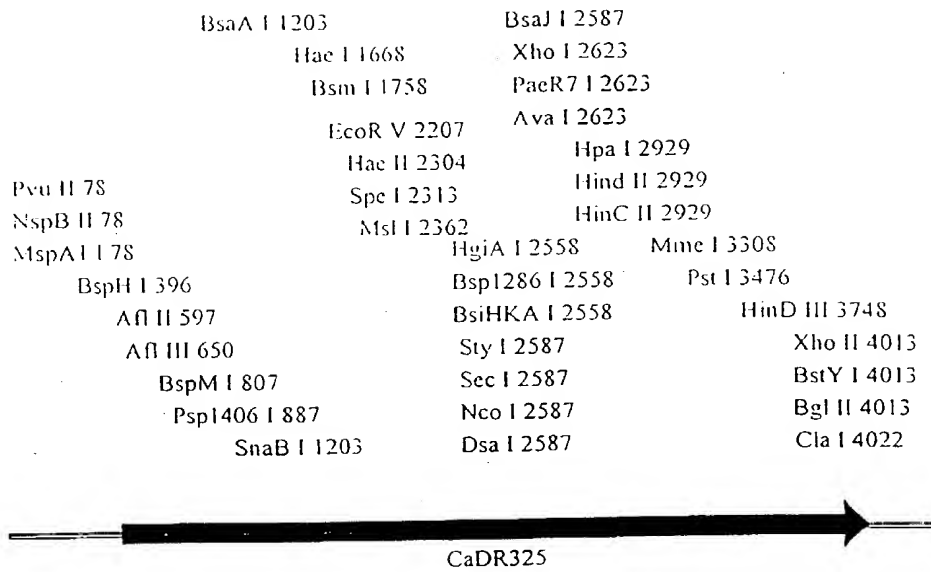
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FIG. 7



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Patent and Trademark Office, U.S. DEPARTMENT OF COMMERCE
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DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION

☒ Declaration OR
Submitted
with Initial Filing

☐ Declaration
Submitted after
Initial Filing

Attorney Docket Number	446.001
First Named Inventor	Jean-Louis LALANNE et al
COMPLETE IF KNOWN	
Application Number	PCT/EP99/07376
Filing Date	September 13, 1999
Group Art Unit	
Examiner Name	

As a below named inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

ESSENTIAL GENES FROM C. ALBICANS AND A METHOD FOR SCREENING
ANTIMYCOTIC SUBSTANCES USING SAID GENES

(Title of the invention)

the specification of which

☐ is attached hereto
OR

☒ was filed on (MM/DD/YYYY) 09/13/99 as United States Application Number or PCT International

Application Number PCT/EP99/07376 and was amended on (MM/DD/YYYY) (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37 Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code §119 (a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or §365 (a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Attached?	
				YES	NO
98402255.8	Europe	09/11/98	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
PCT/EP99/07376 PCT		09/13/99	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

☐ Additional foreign application numbers are listed on a supplemental priority sheet attached hereto:

I hereby claim the benefit under Title 35, United States Code §119(e) of any United States provisional application(s) listed below.

Application Number(s)	Filing Date (MM/DD/YYYY)	<input type="checkbox"/> Additional provisional application numbers are listed on a supplemental priority sheet attached hereto.

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Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

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DECLARATION

I hereby claim the benefit under Title 35, United States Code §120 of any United States application(s), or §365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

U.S. Parent Application Number	PCT Parent Number	Parent Filing Date (MM/DD/YYYY)	Parent Patent Number (if applicable)

☐ Additional U.S. or PCT international application numbers are listed on a supplemental priority sheet attached hereto.

As a named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

Name	Registration Number	Name	Registration Number
Bierman, Muserlian and Lucas	18,818		
Jordan B. Bierman	18,629		
Charles A. Muserlian	19,683		
Donald C. Lucas	31,275		

☐ Additional registered practitioner(s) named on a supplemental sheet attached hereto.

Direct all correspondence to:

Name	Charles A. Muserlian		
Address	Bierman, Muserlian and Lucas		
Address	600 Third Avenue		
City	New York	State	NY
Country	U.S.A.	Telephone	(212) 661-8000
		Fax	(212) 661-8002

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name of Sole or First Inventor:

☐ A petition has been filed for this unsigned inventor

Given Name	Jean-Louis	Middle Initial		Family Name	LALANNE	Suffix e.g. Jr.	
------------	------------	----------------	--	-------------	---------	-----------------	--

Inventor's Signature	<i>JL LALANNE</i>	Date	6 March 2001
----------------------	-------------------	------	--------------

Residence: City	Fontenay sous Bois	State		Country	France	Citizenship	France
-----------------	--------------------	-------	--	---------	--------	-------------	--------

Post Office Address	110, avenue du Maréchal, F-94120 Fontenay sous Bois, France		
---------------------	---	--	--

Post Office Address							
City	Fontenay sous Bois	State		Zip	F-94120	Country	France

☒ Additional inventors are being named on supplemental sheet(s) attached hereto

09766880.060101 (12)

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DECLARATION				ADDITIONAL INVENTOR(S) Supplemental Sheet			
Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor			
Given Name	Corinne	Middle Initial		Family Name	ROCHER	Suffix	
Inventor's Signature				Date	06.02.01		
Residence: City	Paris	State		Country	France	Citizenship	France
Post Office Address	3, rue Elisa Lemonnier, F-75012 Paris, France						
Post Office Address							
City	Paris	State		Zip	F-75012	Country	France
Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor			
Given Name	Thomas	Middle Initial		Family Name	LEUW	Suffix	
Inventor's Signature				Date	7.5.01		
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Post Office Address	Alspitzweg 11, D-86926 Greifenberg, Germany						
Post Office Address							
City	Greifenberg	State		Zip	D-86926	Country	Germany
Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor			
Given Name	Daniel	Middle Initial		Family Name	MARGERIE	Suffix	
Inventor's Signature				Date	02.05.01		
Residence: City	Frankfurt am Main	State		Country	Germany	Citizenship	Germany
Post Office Address	Falkstrasse 104, D-60487 Frankfurt am Main, Germany						
Post Office Address							
City	Frankfurt Main	State		Zip	D-60487	Country	Germany
Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor			
Given Name	Almut	Middle Initial		Family Name	NITSCHKE	Suffix	
Inventor's Signature				Date	07.05.01		
Residence: City	Wiesbaden Krailing	State		Country	Germany	Citizenship	Germany
Post Office Address	Emmanuel Gebelstr. 8 05185 Wiesbaden Bergstrasse 20, D-82152 Krailing, Germany						
Post Office Address							
City	Krailing	State		Zip	D-82152	Country	Germany
<input checked="" type="checkbox"/> Additional inventors are being named on supplemental sheet(s) attached hereto							

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PTO/SB-01 (8-96)
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 Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

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DECLARATION

ADDITIONAL INVENTOR(S)
Supplemental Sheet

Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor			
Given Name	Jutta	Middle Initial		Family Name	REINHARD-RUPP	Suffix	
Inventor's Signature	X J. Reinhard-Rupp DEX				Date	03.05.01	
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Post Office Address		Mussbaumstrasse 25, D-65719 Hopheim, Germany					
Post Office Address		Neufriedenheimer Strasse 82A, D-81375, München, Germany					
City	München Hopheim	State		Zip	D-65719	Country	Germany
Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor			
Given Name	Nicolas	Middle Initial		Family Name	CHALWATZIS	Suffix	
Inventor's Signature	X N. Chalwatzis DEX				Date		
Residence: City	Heppenkeim	State		Country	Germany	Citizenship	Germany
Post Office Address		Krokusweg 15, D-64646 Heppenkeim, Germany					
Post Office Address							
City	Heppenkeim	State		Zip	D-64646	Country	Germany
Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor			
Given Name		Middle Initial		Family Name		Suffix	
Inventor's Signature					Date		
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		Zip		Country	
Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor			
Given Name		Middle Initial		Family Name		Suffix	
Inventor's Signature					Date		
Residence: City		State		Country		Citizenship	
Post Office Address							
Post Office Address							
City		State		Zip		Country	

☐ Additional inventors are being named on supplemental sheet(s) attached hereto

09786880.061101
Rec'd PCT/PTO 06 AUG 2001
09/78 6880
CB
21 Feb 02

SEQUENCE LISTING

<110> AVENTIS PHARMA S.A.

<120> ESSENTIAL GENES FROM C. ALBICANS AND A METHOD FOR
SCREENING ANTIMYCOTIC SUBSTANCES USING SAID GENES

<130> 16655

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<141> 1999-09-13

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<151> 1998-09-11

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Asn Leu Ile Ile Pro His Lys Ser Met Leu Glu Arg Thr Phe Val Leu	
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caa cca tta tgt gaa gta ttg ccc cct gat tat att cat ccc atc agt	1248
Gln Pro Leu Cys Glu Val Leu Pro Pro Asp Tyr Ile His Pro Ile Ser	
405 410 415	
gca gaa agt ttg cat agc cat tta caa caa tta ata aat gat aaa cct	1296
Ala Glu Ser Leu His Ser His Leu Gln Gln Leu Ile Asn Asp Lys Pro	
420 425 430	
caa gag aca gta caa gaa tcg tct gat tta tta caa ttt atc cca gtc	1344
Gln Glu Thr Val Gln Glu Ser Ser Asp Leu Leu Gln Phe Ile Pro Val	
435 440 445	
tct aga ttg cct gtc aaa gat aat att ttg aaa ttt gat caa att aat	1392

Ser	Arg	Leu	Pro	Val	Lys	Asp	Asn	Ile	Leu	Lys	Phe	Asp	Gln	Ile	Asn		
450						455					460						
cat	aaa	tct	cct	act	ttg	att	atg	ggg	ata	ttg	aat	atg	act	cct	gat	1440	
His	Lys	Ser	Pro	Thr	Leu	Ile	Met	Gly	Ile	Leu	Asn	Met	Thr	Pro	Asp		
465					470				475					480			
tca	ttt	agt	gat	ggg	aaa	cat	ttt	gga	aaa	gaa	cta	gat	aat	act		1488	
Ser	Phe	Ser	Asp	Gly	Lys	His	Phe	Gly	Lys	Glu	Leu	Asp	Asn	Thr			
				485				490					495				
gtg	aag	cag	gca	gag	aaa	tta	gtc	agt	gag	ggg	gct	acg	att	att	gac	1536	
Val	Lys	Gln	Ala	Glu	Lys	Leu	Val	Ser	Glu	Gly	Ala	Thr	Ile	Ile	Asp		
			500					505					510				
att	gga	gga	gtt	tcc	aca	cgc	cca	gga	agt	gtt	gaa	ccc	act	gag	gaa	1584	
Ile	Gly	Gly	Val	Ser	Thr	Arg	Pro	Gly	Ser	Val	Glu	Pro	Thr	Glu	Glu		
	515						520					525					
gaa	gaa	ttg	gaa	cgt	gtg	att	cca	tta	att	aaa	gct	att	cgt	caa	tca	1632	
Glu	Glu	Leu	Glu	Arg	Val	Ile	Pro	Leu	Ile	Lys	Ala	Ile	Arg	Gln	Ser		
	530					535					540						
ctg	aac	cct	gat	tta	ctg	aag	gtg	ttg	att	tcg	gtt	gat	act	tat	cgt	1680	
Leu	Asn	Pro	Asp	Leu	Leu	Lys	Val	Leu	Ile	Ser	Val	Asp	Thr	Tyr	Arg		
545					550					555					560		
agg	aac	gtt	gct	gaa	caa	agt	tta	ctt	gtg	ggg	gct	gac	ata	atc	aac	1728	
Arg	Asn	Val	Ala	Glu	Gln	Ser	Leu	Leu	Val	Gly	Ala	Asp	Ile	Ile	Asn		
				565					570					575			
gat	atc	tca	atg	ggc	aaa	tat	gat	gaa	aaa	ata	ttt	gat	gtg	gtt	gct	1776	
Asp	Ile	Ser	Met	Gly	Lys	Tyr	Asp	Glu	Lys	Ile	Phe	Asp	Val	Val	Ala		
				580				585						590			
aaa	tac	gga	tgt	cct	tat	atc	atg	aat	cat	act	cga	gga	tca	cct	aaa	1824	
Lys	Tyr	Gly	Cys	Pro	Tyr	Ile	Met	Asn	His	Thr	Arg	Gly	Ser	Pro	Lys		
		595					600					605					
acc	atg	tct	aaa	ttg	acc	aat	tat	gaa	tca	aat	aca	aat	gat	gat	att	1872	
Thr	Met	Ser	Lys	Leu	Thr	Asn	Tyr	Glu	Ser	Asn	Thr	Asn	Asp	Asp	Ile		
				610			615					620					
atc	gaa	tat	ata	att	gat	cct	aaa	tta	gga	cat	caa	gaa	ttg	gat	ttg	1920	
Ile	Glu	Tyr	Ile	Ile	Asp	Pro	Lys	Leu	Gly	His	Gln	Glu	Leu	Asp	Leu		
625					630					635					640		
tca	cct	gaa	atc	aag	aat	tta	ctc	aat	gga	atc	agt	cgt	gaa	ttg	agt	1968	
Ser	Pro	Glu	Ile	Lys	Asn	Leu	Leu	Asn	Gly	Ile	Ser	Arg	Glu	Leu	Ser		
				645					650					655			
tta	caa	atg	ttt	aaa	gcc	atg	gct	aaa	gga	gtg	aaa	aaa	tgg	caa	att	2016	
Leu	Gln	Met	Phe	Lys	Ala	Met	Ala	Lys	Gly	Val	Lys	Lys	Trp	Gln	Ile		
			660					665					670				
att	ttg	gat	cct	ggg	att	gga	ttt	gct	aaa	aat	ttg	aat	caa	aat	tta	2064	
Ile	Leu	Asp	Pro	Gly	Ile	Gly	Phe	Ala	Lys	Asn	Leu	Asn	Gln	Asn	Leu		

675	680	685	
gca gtt att cgt aat gcc tcg ttt ttt aaa aaa tat tct att caa att			2112
Ala Val Ile Arg Asn Ala Ser Phe Phe Lys Lys Tyr Ser Ile Gln Ile			
690	695	700	
aat gaa cgt gtt gat gat gtg aca atc aaa cat aaa tat tta agt ttt			2160
Asn Glu Arg Val Asp Asp Val Thr Ile Lys His Lys Tyr Leu Ser Phe			
705	710	715	720
aat ggt gct tgt gtt ttg gtg ggg aca tca aga aag aag ttt ttg ggg			2208
Asn Gly Ala Cys Val Leu Val Gly Thr Ser Arg Lys Lys Phe Leu Gly			
725	730	735	
aca tta act ggt aat gaa gtg cct ctg gat cga gta ttt ggc act ggt			2256
Thr Leu Thr Gly Asn Glu Val Pro Leu Asp Arg Val Phe Gly Thr Gly			
740	745	750	
gca aca gtg tct gcg tgt att gaa caa aac act gat att gta aga gtt			2304
Ala Thr Val Ser Ala Cys Ile Glu Gln Asn Thr Asp Ile Val Arg Val			
755	760	765	
cat gat gtt aaa gaa atg aaa gat gta gta tgt ata agt gat gca att			2352
His Asp Val Lys Glu Met Lys Asp Val Val Cys Ile Ser Asp Ala Ile			
770	775	780	
tat aaa aat gta taa			2367
Tyr Lys Asn Val			
785			

<210> 3

<211> 788

<212> PRT

<213> Candida albicans

<400> 3

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Ile	Thr	Gly	Lys	Asp	Ala	Trp	Asn	Arg	Pro	Thr	Pro	Gln	Pro	Ile	Thr
		20						25					30		
Ile	Ser	Leu	Ser	Phe	Asn	Thr	Asp	Phe	His	Lys	Ala	Ser	Glu	Leu	Asp
	35						40					45			
Asn	Leu	Lys	Tyr	Ser	Ile	Asn	Tyr	Ala	Val	Ile	Thr	Arg	Asn	Val	Thr
	50					55					60				
Glu	Phe	Met	Lys	Ser	Asn	Glu	His	Leu	Asn	Phe	Lys	Ser	Leu	Gly	Asn
	65				70					75				80	
Ile	Ala	Gln	Ala	Ile	Ser	Asp	Ile	Gly	Leu	Asp	Gln	Ser	Arg	Gly	Gly
			85					90						95	
Gly	Ser	Ile	Val	Asp	Val	Thr	Ile	Lys	Ser	Leu	Lys	Ser	Glu	Ile	Arg
		100						105					110		

Ala Glu Ser Val Glu Tyr Lys Ile Asn Arg Asn Thr Leu Gly Gln Pro
 115 120 125
 Val Pro Leu Asp Ile Phe Gln Val Asn Lys Leu Arg Leu Leu Thr Ile
 130 135 140
 Ile Gly Val Phe Thr Phe Glu Arg Leu Gln Lys Gln Ile Val Asp Val
 145 150 155 160
 Asp Leu Gln Phe Lys Ile Glu Pro Asn Ser Asn Leu Tyr Phe His Gln
 165 170 175
 Ile Ile Ala Asp Ile Val Ser Tyr Val Glu Ser Ser Asn Phe Lys Thr
 180 185 190
 Val Glu Ala Leu Val Ser Lys Ile Gly Gln Leu Thr Phe Gln Lys Tyr
 195 200 205
 Asp Gly Val Ala Glu Val Val Ala Thr Val Thr Lys Pro Asn Ala Phe
 210 215 220
 Ser His Val Glu Gly Val Gly Val Ser Ser Thr Met Val Lys Asp Asn
 225 230 235 240
 Phe Lys Asp Met Glu Pro Val Lys Phe Glu Asn Thr Ile Ala Gln Thr
 245 250 255
 Asn Arg Ala Phe Asn Leu Pro Val Glu Asn Glu Lys Thr Glu Asp Tyr
 260 265 270
 Thr Gly Tyr His Thr Ala Phe Ile Ala Phe Gly Ser Asn Thr Gly Asn
 275 280 285
 Gln Val Glu Asn Ile Thr Asn Ser Phe Glu Leu Leu Gln Lys Tyr Gly
 290 295 300
 Ile Thr Ile Glu Ala Thr Ser Ser Leu Tyr Ile Ser Lys Pro Met Tyr
 305 310 315 320
 Tyr Leu Asp Gln Pro Asp Phe Phe Asn Gly Val Ile Lys Val Asn Phe
 325 330 335
 Gln Asn Ile Ser Pro Phe Gln Leu Leu Lys Ile Leu Lys Asp Ile Glu
 340 345 350
 Tyr Lys His Leu Glu Arg Lys Lys Asp Phe Asp Asn Gly Pro Arg Ser
 355 360 365
 Ile Asp Leu Asp Ile Ile Leu Tyr Asp Asp Leu Gln Leu Asn Thr Glu
 370 375 380
 Asn Leu Ile Ile Pro His Lys Ser Met Leu Glu Arg Thr Phe Val Leu
 385 390 395 400
 Gln Pro Leu Cys Glu Val Leu Pro Pro Asp Tyr Ile His Pro Ile Ser
 405 410 415

Ala Glu Ser Leu His Ser His Leu Gln Gln Leu Ile Asn Asp Lys Pro
 420 425 430
 Gln Glu Thr Val Gln Glu Ser Ser Asp Leu Leu Gln Phe Ile Pro Val
 435 440 445
 Ser Arg Leu Pro Val Lys Asp Asn Ile Leu Lys Phe Asp Gln Ile Asn
 450 455 460
 His Lys Ser Pro Thr Leu Ile Met Gly Ile Leu Asn Met Thr Pro Asp
 465 470 475 480
 Ser Phe Ser Asp Gly Gly Lys His Phe Gly Lys Glu Leu Asp Asn Thr
 485 490 495
 Val Lys Gln Ala Glu Lys Leu Val Ser Glu Gly Ala Thr Ile Ile Asp
 500 505 510
 Ile Gly Gly Val Ser Thr Arg Pro Gly Ser Val Glu Pro Thr Glu Glu
 515 520 525
 Glu Glu Leu Glu Arg Val Ile Pro Leu Ile Lys Ala Ile Arg Gln Ser
 530 535 540
 Leu Asn Pro Asp Leu Leu Lys Val Leu Ile Ser Val Asp Thr Tyr Arg
 545 550 555 560
 Arg Asn Val Ala Glu Gln Ser Leu Leu Val Gly Ala Asp Ile Ile Asn
 565 570 575
 Asp Ile Ser Met Gly Lys Tyr Asp Glu Lys Ile Phe Asp Val Val Ala
 580 585 590
 Lys Tyr Gly Cys Pro Tyr Ile Met Asn His Thr Arg Gly Ser Pro Lys
 595 600 605
 Thr Met Ser Lys Leu Thr Asn Tyr Glu Ser Asn Thr Asn Asp Asp Ile
 610 615 620
 Ile Glu Tyr Ile Ile Asp Pro Lys Leu Gly His Gln Glu Leu Asp Leu
 625 630 635 640
 Ser Pro Glu Ile Lys Asn Leu Leu Asn Gly Ile Ser Arg Glu Leu Ser
 645 650 655
 Leu Gln Met Phe Lys Ala Met Ala Lys Gly Val Lys Lys Trp Gln Ile
 660 665 670
 Ile Leu Asp Pro Gly Ile Gly Phe Ala Lys Asn Leu Asn Gln Asn Leu
 675 680 685
 Ala Val Ile Arg Asn Ala Ser Phe Phe Lys Lys Tyr Ser Ile Gln Ile
 690 695 700
 Asn Glu Arg Val Asp Asp Val Thr Ile Lys His Lys Tyr Leu Ser Phe
 705 710 715 720

Asn Gly Ala Cys Val Leu Val Gly Thr Ser Arg Lys Lys Phe Leu Gly
 725 730 735

Thr Leu Thr Gly Asn Glu Val Pro Leu Asp Arg Val Phe Gly Thr Gly
 740 745 750

Ala Thr Val Ser Ala Cys Ile Glu Gln Asn Thr Asp Ile Val Arg Val
 755 760 765

His Asp Val Lys Glu Met Lys Asp Val Val Cys Ile Ser Asp Ala Ile
 770 775 780

Tyr Lys Asn Val
 785

<210> 4

<211> 647

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Probe

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 aaaaaaatgt gggattctca attacaatca ttatttaaac atgttgacgg tgcataaaa 120
 tttgtgcaac cattacccaa tagacacatt gtcgcggaaa gtggacgatg gtttgaagtt 180
 aatgtgggga attggaaacc aagttatcca actcatttat ttatatttaa tgatttaatt 240
 ttaattgccg ttaaaaaatc atcatctagt agtcaggaac ctactacagg gggaagtaat 300
 ggtggttcaa aatcgagatt acaagcgggt caatgttggc ccttaactca agtatcatta 360
 caacaaatca aatcacgaa aaaagatgac gataagatgt attttatcaa tcttaaatcc 420
 aaatctttaa gttatgtata cctgacggat cgttatgac attttgtgaa agttacggaa 480
 gcatttaata aaggtagaaa tgaaatgatt caaagtgaat gattattaga ttcaagactt 540
 tcatctcctt caaataataa tggagattct aaagaagaga aacgacaatt acgggaatca 600
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<210> 5

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<212> DNA

<213> Candida albicans

<220>

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<223> gene CaBR102

<400> 5

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1 5 10 15	
aac agg aaa agc agg gct gta tgg cag aat aac aac act tct act cat	96
Asn Arg Lys Ser Arg Ala Val Trp Gln Asn Asn Asn Thr Ser Thr His	
20 25 30	
aat aat cct tat gct aat tta agc act ggt gaa aaa agt agg agt cgc	144
Asn Asn Pro Tyr Ala Asn Leu Ser Thr Gly Glu Lys Ser Arg Ser Arg	
35 40 45	
cat aac act ggt agt tct tat gtt tct cca tat ggc ggc ggt aat gga	192
His Asn Thr Gly Ser Ser Tyr Val Ser Pro Tyr Gly Gly Gly Asn Gly	
50 55 60	
gag gag aat gct tat act ggg aat aac aac aaa tca aat act agt ggt	240
Glu Glu Asn Ala Tyr Thr Gly Asn Asn Asn Lys Ser Asn Thr Ser Gly	
65 70 75 80	
aat tta tta caa gtt cct gga gca gga gga gga gga gat ttg aat tct	288
Asn Leu Leu Gln Val Pro Gly Ala Gly Gly Gly Gly Asp Leu Asn Ser	
85 90 95	
aat aag aaa caa agt cga aga atg agt att cat gta tca gct cgt caa	336
Asn Lys Lys Gln Ser Arg Arg Met Ser Ile His Val Ser Ala Arg Gln	
100 105 110	
cat gga aga tca ttt tca caa act ggt cca att gat atg gca aat tta	384
His Gly Arg Ser Phe Ser Gln Thr Gly Pro Ile Asp Met Ala Asn Leu	
115 120 125	
ccg gca tta cct aaa ata ggt ggt gtt act act agt ggt gtt ggc ggt	432
Pro Ala Leu Pro Lys Ile Gly Gly Val Thr Thr Ser Gly Val Gly Gly	
130 135 140	
gct ggt ggt gat gtt atg aca agg act ggg gga ttg acg ata gaa caa	480
Ala Gly Gly Asp Val Met Thr Arg Thr Gly Gly Leu Thr Ile Glu Gln	
145 150 155 160	
aaa ata ttc aaa gaa tta agt caa gga tca gca gct gaa gtt gat gat	528
Lys Ile Phe Lys Glu Leu Ser Gln Gly Ser Ala Ala Glu Val Asp Asp	
165 170 175	
tat tac aag aca tta ttg aaa cag aaa aat tta atc act cgt gac att	576
Tyr Tyr Lys Thr Leu Leu Lys Gln Lys Asn Leu Ile Thr Arg Asp Ile	
180 185 190	
aag gat aat att aat cag aat caa aaa aat att tta caa tta aca aaa	624
Lys Asp Asn Ile Asn Gln Asn Gln Lys Asn Ile Leu Gln Leu Thr Lys	

195	200	205	
gac ttg aaa gag acc caa gaa gaa ttg att gaa ttg aga gga acc act Asp Leu Lys Glu Thr Gln Glu Glu Leu Ile Glu Leu Arg Gly Thr Thr 210 215 220			672
aaa gaa tta tat gaa gtt tta ggt tat ttc aaa gaa tca gct caa cgt Lys Glu Leu Tyr Glu Val Leu Gly Tyr Phe Lys Glu Ser Ala Gln Arg 225 230 235 240			720
aga tta gaa ttg gaa ttt gaa cca gaa aca caa aaa gaa ctt cat ctg Arg Leu Glu Leu Glu Phe Glu Pro Glu Thr Gln Lys Glu Leu His Leu 245 250 255			768
cct caa aaa agt aat caa ttg ggt att cct agt aat aaa aag aaa gat Pro Gln Lys Ser Asn Gln Leu Gly Ile Pro Ser Asn Lys Lys Lys Asp 260 265 270			816
cga tca tca att atg gtg ctt aaa aaa atg tgg gat tct caa tta caa Arg Ser Ser Ile Met Val Leu Lys Lys Met Trp Asp Ser Gln Leu Gln 275 280 285			864
tca tta ttt aaa cat gtt gac ggt gca tca aaa ttt gtc caa cca tta Ser Leu Phe Lys His Val Asp Gly Ala Ser Lys Phe Val Gln Pro Leu 290 295 300			912
ccc aat aga cac att gtc gcg gaa agt gga cga tgg ttt gaa gtt aat Pro Asn Arg His Ile Val Ala Glu Ser Gly Arg Trp Phe Glu Val Asn 305 310 315 320			960
gtg ggg aat tgg aaa cca agt tat cca act cat tta ttt ata ttt aat Val Gly Asn Trp Lys Pro Ser Tyr Pro Thr His Leu Phe Ile Phe Asn 325 330 335			1008
gat tta att tta att act gtt aaa aaa tca tca tct agt agt cag gaa Asp Leu Ile Leu Ile Thr Val Lys Lys Ser Ser Ser Ser Ser Gln Glu 340 345 350			1056
cct act aca ggg gga agt aat ggt ggt tca aaa tcg aga tta caa gcg Pro Thr Thr Gly Gly Ser Asn Gly Gly Ser Lys Ser Arg Leu Gln Ala 355 360 365			1104
gtt caa tgt tgg ccc tta act caa gta tca tta caa caa atc aaa tca Val Gln Cys Trp Pro Leu Thr Gln Val Ser Leu Gln Gln Ile Lys Ser 370 375 380			1152
ccg aaa aaa gat gac gat aag atg tat ttt atc aat ctt aaa tcc aaa Pro Lys Lys Asp Asp Lys Met Tyr Phe Ile Asn Leu Lys Ser Lys 385 390 395 400			1200
tct tta agt tat gta tac ctg acg gat cgt tat gat cat ttt gtg aaa Ser Leu Ser Tyr Val Tyr Leu Thr Asp Arg Tyr Asp His Phe Val Lys 405 410 415			1248
gtt acg gaa gca ttt aat aaa ggt aga aat gaa atg att caa agt gaa Val Thr Glu Ala Phe Asn Lys Gly Arg Asn Glu Met Ile Gln Ser Glu 420 425 430			1296

aga tta tta gat tca aga ctt tca tct cct tca aat aat aat gga gat	1344
Arg Leu Leu Asp Ser Arg Leu Ser Ser Pro Ser Asn Asn Asn Gly Asp	
435 440 445	
tct aaa gaa gag aaa cga caa tta cgg gaa tca tta aga aac tca ggc	1392
Ser Lys Glu Glu Lys Arg Gln Leu Arg Glu Ser Leu Arg Asn Ser Gly	
450 455 460	
aat tat aaa gaa gga gtt act gat gat gcc ggt gga gct gca act ggt	1440
Asn Tyr Lys Glu Gly Val Thr Asp Asp Ala Gly Gly Ala Ala Thr Gly	
465 470 475 480	
ggt ggt agg aaa agt gcc ggt act cct aat aga aat agt act gat tac	1488
Gly Gly Arg Lys Ser Ala Gly Thr Pro Asn Arg Asn Ser Thr Asp Tyr	
485 490 495	
ggt tta cat gat ata tct gct cga gta cat tca cgt aat cga tca caa	1536
Val Leu His Asp Ile Ser Ala Arg Val His Ser Arg Asn Arg Ser Gln	
500 505 510	
gat tta ggg aat aat ttc aaa tta gct aat aat ggg aaa tca caa ttt	1584
Asp Leu Gly Asn Asn Phe Lys Leu Ala Asn Asn Gly Lys Ser Gln Phe	
515 520 525	
ttc aat gaa atc aaa act tta gaa gat cga tta gat gat gtt gac gtt	1632
Phe Asn Glu Ile Lys Thr Leu Glu Asp Arg Leu Asp Asp Val Asp Val	
530 535 540	
gaa ata tcg cat aat caa tat gct gaa gcc gtg gaa tta ata tca ata	1680
Glu Ile Ser His Asn Gln Tyr Ala Glu Ala Val Glu Leu Ile Ser Ile	
545 550 555 560	
att gaa tct aaa tta cgt aat att gaa aat gca tta act aat caa cgt	1728
Ile Glu Ser Lys Leu Arg Asn Ile Glu Asn Ala Leu Thr Asn Gln Arg	
565 570 575	
aat gga ggt aaa aat gtc aat att gct gat gaa tta tta ctt tta gat	1776
Asn Gly Gly Lys Asn Val Asn Ile Ala Asp Glu Leu Leu Leu Leu Asp	
580 585 590	
gta tca aaa ttg aaa att aaa aat cgg aaa gaa aat gta tct aat gga	1824
Val Ser Lys Leu Lys Ile Lys Asn Arg Lys Glu Asn Val Ser Asn Gly	
595 600 605	
tta ata ttt gat tta caa cat aat ata gct aaa ctt aaa caa gat gat	1872
Leu Ile Phe Asp Leu Gln His Asn Ile Ala Lys Leu Lys Gln Asp Asp	
610 615 620	
att gat aat att ttg acg tta ttt gat aat tta gag caa tta gat cga	1920
Ile Asp Asn Ile Leu Thr Leu Phe Asp Asn Leu Glu Gln Leu Asp Arg	
625 630 635 640	
ggg gtt caa gga tat ttg gat tca atg tca gct tat tta tca act aca	1968
Gly Val Gln Gly Tyr Leu Asp Ser Met Ser Ala Tyr Leu Ser Thr Thr	
645 650 655	

gta tca aaa tta att gtt ggt tta caa gga tca acg aaa atc gat gtt 2016
 Val Ser Lys Leu Ile Val Gly Leu Gln Gly Ser Thr Lys Ile Asp Val
 660 665 670

gtt aat tat ctt tcc aat tta atg gtt att aat gta tct att gtg aaa 2064
 Val Asn Tyr Leu Ser Asn Leu Met Val Ile Asn Val Ser Ile Val Lys
 675 680 685

cgt aca att caa act tat gaa caa ata att gct cca att tta aaa cgt 2112
 Arg Thr Ile Gln Thr Tyr Glu Gln Ile Ile Ala Pro Ile Leu Lys Arg
 690 695 700

cat ggt gat gtt gat tca agt gga ttg att aat tgg tgt att gat gaa 2160
 His Gly Asp Val Asp Ser Ser Gly Leu Ile Asn Trp Cys Ile Asp Glu
 705 710 715 720

ttt act aaa ctt tgt aaa caa att aaa aaa cat ttg tat gga aca ttg 2208
 Phe Thr Lys Leu Cys Lys Gln Ile Lys Lys His Leu Tyr Gly Thr Leu
 725 730 735

ttg ata tct tct ggg att aat atg gaa act gat gaa cca att tat aaa 2256
 Leu Ile Ser Ser Gly Ile Asn Met Glu Thr Asp Glu Pro Ile Tyr Lys
 740 745 750

gtt aaa gaa aga aaa tta tat gat aat ttc ttg aag att atg caa cca 2304
 Val Lys Glu Arg Lys Leu Tyr Asp Asn Phe Leu Lys Ile Met Gln Pro
 755 760 765

caa ttg gaa gaa tta aaa ctg gtg gga tta aat gtt gat tat ata ttt 2352
 Gln Leu Glu Glu Leu Lys Leu Val Gly Leu Asn Val Asp Tyr Ile Phe
 770 775 780

gag tct ata tta aat ctt gaa 2373
 Glu Ser Ile Leu Asn Leu Glu
 785 790

<210> 6

<211> 791

<212> PRT

<213> Candida albicans

<400> 6

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Asn Arg Lys Ser Arg Ala Val Trp Gln Asn Asn Asn Thr Ser Thr His
 20 25 30

Asn Asn Pro Tyr Ala Asn Leu Ser Thr Gly Glu Lys Ser Arg Ser Arg
 35 40 45

His Asn Thr Gly Ser Ser Tyr Val Ser Pro Tyr Gly Gly Gly Asn Gly
 50 55 60

Glu Glu Asn Ala Tyr Thr Gly Asn Asn Asn Lys Ser Asn Thr Ser Gly
 65 70 75 80

Asn Leu Leu Gln Val Pro Gly Ala Gly Gly Gly Gly Asp Leu Asn Ser
 85 90 95

Asn Lys Lys Gln Ser Arg Arg Met Ser Ile His Val Ser Ala Arg Gln
 100 105 110

His Gly Arg Ser Phe Ser Gln Thr Gly Pro Ile Asp Met Ala Asn Leu
 115 120 125

Pro Ala Leu Pro Lys Ile Gly Gly Val Thr Thr Ser Gly Val Gly Gly
 130 135 140

Ala Gly Gly Asp Val Met Thr Arg Thr Gly Gly Leu Thr Ile Glu Gln
 145 150 155 160

Lys Ile Phe Lys Glu Leu Ser Gln Gly Ser Ala Ala Glu Val Asp Asp
 165 170 175

Tyr Tyr Lys Thr Leu Leu Lys Gln Lys Asn Leu Ile Thr Arg Asp Ile
 180 185 190

Lys Asp Asn Ile Asn Gln Asn Gln Lys Asn Ile Leu Gln Leu Thr Lys
 195 200 205

Asp Leu Lys Glu Thr Gln Glu Glu Leu Ile Glu Leu Arg Gly Thr Thr
 210 215 220

Lys Glu Leu Tyr Glu Val Leu Gly Tyr Phe Lys Glu Ser Ala Gln Arg
 225 230 235 240

Arg Leu Glu Leu Glu Phe Glu Pro Glu Thr Gln Lys Glu Leu His Leu
 245 250 255

Pro Gln Lys Ser Asn Gln Leu Gly Ile Pro Ser Asn Lys Lys Lys Asp
 260 265 270

Arg Ser Ser Ile Met Val Leu Lys Lys Met Trp Asp Ser Gln Leu Gln
 275 280 285

Ser Leu Phe Lys His Val Asp Gly Ala Ser Lys Phe Val Gln Pro Leu
 290 295 300

Pro Asn Arg His Ile Val Ala Glu Ser Gly Arg Trp Phe Glu Val Asn
 305 310 315 320

Val Gly Asn Trp Lys Pro Ser Tyr Pro Thr His Leu Phe Ile Phe Asn
 325 330 335

Asp Leu Ile Leu Ile Thr Val Lys Lys Ser Ser Ser Ser Ser Gln Glu
 340 345 350

Pro Thr Thr Gly Gly Ser Asn Gly Gly Ser Lys Ser Arg Leu Gln Ala
 355 360 365

Val Gln Cys Trp Pro Leu Thr Gln Val Ser Leu Gln Gln Ile Lys Ser
 370 375 380

Pro Lys Lys Asp Asp Asp Lys Met Tyr Phe Ile Asn Leu Lys Ser Lys
 385 390 395 400
 Ser Leu Ser Tyr Val Tyr Leu Thr Asp Arg Tyr Asp His Phe Val Lys
 405 410 415
 Val Thr Glu Ala Phe Asn Lys Gly Arg Asn Glu Met Ile Gln Ser Glu
 420 425 430
 Arg Leu Leu Asp Ser Arg Leu Ser Ser Pro Ser Asn Asn Asn Gly Asp
 435 440 445
 Ser Lys Glu Glu Lys Arg Gln Leu Arg Glu Ser Leu Arg Asn Ser Gly
 450 455 460
 Asn Tyr Lys Glu Gly Val Thr Asp Asp Ala Gly Gly Ala Ala Thr Gly
 465 470 475 480
 Gly Gly Arg Lys Ser Ala Gly Thr Pro Asn Arg Asn Ser Thr Asp Tyr
 485 490 495
 Val Leu His Asp Ile Ser Ala Arg Val His Ser Arg Asn Arg Ser Gln
 500 505 510
 Asp Leu Gly Asn Asn Phe Lys Leu Ala Asn Asn Gly Lys Ser Gln Phe
 515 520 525
 Phe Asn Glu Ile Lys Thr Leu Glu Asp Arg Leu Asp Asp Val Asp Val
 530 535 540
 Glu Ile Ser His Asn Gln Tyr Ala Glu Ala Val Glu Leu Ile Ser Ile
 545 550 555 560
 Ile Glu Ser Lys Leu Arg Asn Ile Glu Asn Ala Leu Thr Asn Gln Arg
 565 570 575
 Asn Gly Gly Lys Asn Val Asn Ile Ala Asp Glu Leu Leu Leu Leu Asp
 580 585 590
 Val Ser Lys Leu Lys Ile Lys Asn Arg Lys Glu Asn Val Ser Asn Gly
 595 600 605
 Leu Ile Phe Asp Leu Gln His Asn Ile Ala Lys Leu Lys Gln Asp Asp
 610 615 620
 Ile Asp Asn Ile Leu Thr Leu Phe Asp Asn Leu Glu Gln Leu Asp Arg
 625 630 635 640
 Gly Val Gln Gly Tyr Leu Asp Ser Met Ser Ala Tyr Leu Ser Thr Thr
 645 650 655
 Val Ser Lys Leu Ile Val Gly Leu Gln Gly Ser Thr Lys Ile Asp Val
 660 665 670
 Val Asn Tyr Leu Ser Asn Leu Met Val Ile Asn Val Ser Ile Val Lys
 675 680 685

Arg Thr Ile Gln Thr Tyr Glu Gln Ile Ile Ala Pro Ile Leu Lys Arg
690 695 700

His Gly Asp Val Asp Ser Ser Gly Leu Ile Asn Trp Cys Ile Asp Glu
705 710 715 720

Phe Thr Lys Leu Cys Lys Gln Ile Lys Lys His Leu Tyr Gly Thr Leu
725 730 735

Leu Ile Ser Ser Gly Ile Asn Met Glu Thr Asp Glu Pro Ile Tyr Lys
740 745 750

Val Lys Glu Arg Lys Leu Tyr Asp Asn Phe Leu Lys Ile Met Gln Pro
755 760 765

Gln Leu Glu Glu Leu Lys Leu Val Gly Leu Asn Val Asp Tyr Ile Phe
770 775 780

Glu Ser Ile Leu Asn Leu Glu
785 790

<210> 7

<211> 343

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Probe

<400> 7

ctgcagtaaa cctccagat ataacagact ctttatgtcc agtgatttcg ccaacaaatc 60
ttgggtggttg ggtgtgtgtg gtccataagt atgcogtgtt gtcaccaccc ccagtcaata 120
ccattggcaa tttaggatgt gaaaaaatag taaatatact atcggtatgt ttatcaaaat 180
aagtccatga attgttggaac atgtcaattt cttaaagtctc atgctcatca tetaattcca 240
tctctcctc tcttctcatcg ggtggcgctt gatcatcctc tgcaacttcc tcagccactt 300
cattaacatt gatataattct tcttgagtat cgtctacgac gtc 343

<210> 8

<211> 1248

<212> DNA

<213> Candida albicans

<220>

<221> CDS

<222> (1)..(1245)

<220>

<221> gene

<222> (1)..(1245)

<223> gene CaIR012

<400> 8

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Met Ser His Gln Gln Glu Asp Val Val Asp Asp Thr Gln Glu Glu Tyr	
1 5 10 15	
atc aat gtt aat gaa gtg gct gag gaa gtt gca gat gat gat caa gcg	96
Ile Asn Val Asn Glu Val Ala Glu Glu Val Ala Asp Asp Asp Gln Ala	
20 25 30	
cca ccc gat gaa gaa gat gag gag atg gaa tta gat gat gag cat gag	144
Pro Pro Asp Glu Glu Asp Glu Glu Met Glu Leu Asp Asp Glu His Glu	
35 40 45	
act tta gaa att gac atg tcc aac aat tca tgg act tat ttt gat aaa	192
Thr Leu Glu Ile Asp Met Ser Asn Asn Ser Trp Thr Tyr Phe Asp Lys	
50 55 60	
cat acc gat agt ata ttt act att ttt tca cat cct aaa ttg cca atg	240
His Thr Asp Ser Ile Phe Thr Ile Phe Ser His Pro Lys Leu Pro Met	
65 70 75 80	
gta ttg act ggg ggt ggt gac aac acg gca tac tta tgg acc aca cac	288
Val Leu Thr Gly Gly Gly Asp Asn Thr Ala Tyr Leu Trp Thr Thr His	
85 90 95	
acc caa cca cca aga ttt gtt ggc gaa atc act gga cat aaa gag tct	336
Thr Gln Pro Pro Arg Phe Val Gly Glu Ile Thr Gly His Lys Glu Ser	
100 105 110	
gtt ata tct gga ggg ttt act gca gac ggc aag ttt gtt gtt act gca	384
Val Ile Ser Gly Gly Phe Thr Ala Asp Gly Lys Phe Val Val Thr Ala	
115 120 125	
gac atg aat gga tta att caa gtt ttc aaa gcc aca aaa gga ggt gaa	432
Asp Met Asn Gly Leu Ile Gln Val Phe Lys Ala Thr Lys Gly Gly Glu	
130 135 140	
cag tgg gtg aaa ttt ggt gaa ttg gac gaa gtt gaa gaa gtg ttg ttt	480
Gln Trp Val Lys Phe Gly Glu Leu Asp Glu Val Glu Glu Val Leu Phe	
145 150 155 160	
gtt act gtg cat cca aca tta cca ttc ttt gcc ttt ggt gct acc gat	528
Val Thr Val His Pro Thr Leu Pro Phe Phe Ala Phe Gly Ala Thr Asp	
165 170 175	
gga tct ata tgg gtc tac caa ata gac gaa tcc agt aaa ctg cta gtg	576
Gly Ser Ile Trp Val Tyr Gln Ile Asp Glu Ser Ser Lys Leu Leu Val	
180 185 190	
caa att atg tct ggg ttc tca cac aca tta gaa tgt aat ggt gct gta	624
Gln Ile Met Ser Gly Phe Ser His Thr Leu Glu Cys Asn Gly Ala Val	
195 200 205	
ttt ata caa gga aaa gat gaa aat gat ttg aca ttg gtc tct ata agt	672
Phe Ile Gln Gly Lys Asp Glu Asn Asp Leu Thr Leu Val Ser Ile Ser	

210	215	220	
gaa gat ggt act gtg gtg aac tgg aac tgt ttt aca gga caa gtg aat			720
Glu Asp Gly Thr Val Val Asn Trp Asn Cys Phe Thr Gly Gln Val Asn			
225	230	235	240
tat aaa ttg caa cct cat gat gac ttt aaa gga gtt gaa agt ccg tgg			768
Tyr Lys Leu Gln Pro His Asp Asp Phe Lys Gly Val Glu Ser Pro Trp			
	245	250	255
gtc acg gtc aaa gta cat ggt aat ctt gtg gcc att ggt ggc aga gat			816
Val Thr Val Lys Val His Gly Asn Leu Val Ala Ile Gly Gly Arg Asp			
	260	265	270
ggc cag cta tca att gtg aac aat gac act ggt aaa atc gtt cat act			864
Gly Gln Leu Ser Ile Val Asn Asn Asp Thr Gly Lys Ile Val His Thr			
	275	280	285
ctt aaa aca ttg gat aat gtc gac gac att gca gaa ctc tca att gag			912
Leu Lys Thr Leu Asp Asn Val Asp Asp Ile Ala Glu Leu Ser Ile Glu			
	290	295	300
gca ttg agt tgg tgt gaa agc aaa aat att aac ctc ttg gca gtg ggt			960
Ala Leu Ser Trp Cys Glu Ser Lys Asn Ile Asn Leu Leu Ala Val Gly			
305	310	315	320
ttg gtt tct ggt gac gtt tta tta ttt gat act cag caa tgg aga ttg			1008
Leu Val Ser Gly Asp Val Leu Leu Phe Asp Thr Gln Gln Trp Arg Leu			
	325	330	335
aga aag aac ttg aaa gtt gac gat gcc atc acc aaa tta caa ttt gtt			1056
Arg Lys Asn Leu Lys Val Asp Asp Ala Ile Thr Lys Leu Gln Phe Val			
	340	345	350
ggc gaa acc ccc att ttg gtg gga agt agt atg gat ggt aaa att tac			1104
Gly Glu Thr Pro Ile Leu Val Gly Ser Ser Met Asp Gly Lys Ile Tyr			
	355	360	365
aaa tgg gac gct aga act ggt gaa gag ttg ttt gct ggt gtg gga cac			1152
Lys Trp Asp Ala Arg Thr Gly Glu Glu Leu Phe Ala Gly Val Gly His			
	370	375	380
aac atg gga gta ttg gac ttt gct att tta gat gga ggt aaa aag ttg			1200
Asn Met Gly Val Leu Asp Phe Ala Ile Leu Asp Gly Gly Lys Lys Leu			
385	390	395	400
gtt act gct ggt gat gaa ggt gtt tca ttg gtc ttt gta cat gaa tag			1248
Val Thr Ala Gly Asp Glu Gly Val Ser Leu Val Phe Val His Glu			
	405	410	415

<210> 9

<211> 415

<212> PRT

<213> Candida albicans

<400> 9

Met Ser His Gln Gln Glu Asp Val Val Asp Asp Thr Gln Glu Glu Tyr
 1 5 10 15
 Ile Asn Val Asn Glu Val Ala Glu Glu Val Ala Asp Asp Asp Gln Ala
 20 25 30
 Pro Pro Asp Glu Glu Asp Glu Glu Met Glu Leu Asp Asp Glu His Glu
 35 40 45
 Thr Leu Glu Ile Asp Met Ser Asn Asn Ser Trp Thr Tyr Phe Asp Lys
 50 55 60
 His Thr Asp Ser Ile Phe Thr Ile Phe Ser His Pro Lys Leu Pro Met
 65 70 75 80
 Val Leu Thr Gly Gly Gly Asp Asn Thr Ala Tyr Leu Trp Thr Thr His
 85 90 95
 Thr Gln Pro Pro Arg Phe Val Gly Glu Ile Thr Gly His Lys Glu Ser
 100 105 110
 Val Ile Ser Gly Gly Phe Thr Ala Asp Gly Lys Phe Val Val Thr Ala
 115 120 125
 Asp Met Asn Gly Leu Ile Gln Val Phe Lys Ala Thr Lys Gly Gly Glu
 130 135 140
 Gln Trp Val Lys Phe Gly Glu Leu Asp Glu Val Glu Glu Val Leu Phe
 145 150 155 160
 Val Thr Val His Pro Thr Leu Pro Phe Phe Ala Phe Gly Ala Thr Asp
 165 170 175
 Gly Ser Ile Trp Val Tyr Gln Ile Asp Glu Ser Ser Lys Leu Leu Val
 180 185 190
 Gln Ile Met Ser Gly Phe Ser His Thr Leu Glu Cys Asn Gly Ala Val
 195 200 205
 Phe Ile Gln Gly Lys Asp Glu Asn Asp Leu Thr Leu Val Ser Ile Ser
 210 215 220
 Glu Asp Gly Thr Val Val Asn Trp Asn Cys Phe Thr Gly Gln Val Asn
 225 230 235 240
 Tyr Lys Leu Gln Pro His Asp Asp Phe Lys Gly Val Glu Ser Pro Trp
 245 250 255
 Val Thr Val Lys Val His Gly Asn Leu Val Ala Ile Gly Gly Arg Asp
 260 265 270
 Gly Gln Leu Ser Ile Val Asn Asn Asp Thr Gly Lys Ile Val His Thr
 275 280 285
 Leu Lys Thr Leu Asp Asn Val Asp Asp Ile Ala Glu Leu Ser Ile Glu
 290 295 300

Ala Leu Ser Trp Cys Glu Ser Lys Asn Ile Asn Leu Leu Ala Val Gly
 305 310 315 320

Leu Val Ser Gly Asp Val Leu Leu Phe Asp Thr Gln Gln Trp Arg Leu
 325 330 335

Arg Lys Asn Leu Lys Val Asp Asp Ala Ile Thr Lys Leu Gln Phe Val
 340 345 350

Gly Glu Thr Pro Ile Leu Val Gly Ser Ser Met Asp Gly Lys Ile Tyr
 355 360 365

Lys Trp Asp Ala Arg Thr Gly Glu Glu Leu Phe Ala Gly Val Gly His
 370 375 380

Asn Met Gly Val Leu Asp Phe Ala Ile Leu Asp Gly Gly Lys Lys Leu
 385 390 395 400

Val Thr Ala Gly Asp Glu Gly Val Ser Leu Val Phe Val His Glu
 405 410 415

<210> 10

<211> 5544

<212> DNA

<213> Candida albicans

<220>

<221> CDS

<222> (1)..(5541)

<220>

<221> gene

<222> (1)..(5541)

<223> gene CaJL039

<400> 10

atg agt ggc ata ttt aat tgg tcg ctg gat gtg ttt gcc gat att tat 48
 Met Ser Gly Ile Phe Asn Trp Ser Leu Asp Val Phe Ala Asp Ile Tyr
 1 5 10 15

aac acc ctc aag ttt gag tcc aat ata gat ttg gat aca atc gac ttc 96
 Asn Thr Leu Lys Phe Glu Ser Asn Ile Asp Leu Asp Thr Ile Asp Phe
 20 25 30

acc agc atc aag aat gat ctt gca aat gtt ttg att aca cca gtc cct 144
 Thr Ser Ile Lys Asn Asp Leu Ala Asn Val Leu Ile Thr Pro Val Pro
 35 40 45

ctg gat caa tca cgt agc aaa ctt gga gac gca tca aaa cca gtg gcg 192
 Leu Asp Gln Ser Arg Ser Lys Leu Gly Asp Ala Ser Lys Pro Val Ala
 50 55 60

ttg ccc agt gga gat gag gtg aaa ttg aat caa gca tca att gaa att 240
 Leu Pro Ser Gly Asp Glu Val Lys Leu Asn Gln Ala Ser Ile Glu Ile
 65 70 75 80

act gga gtt tta tca aat gaa ttg gat tta gat gaa cta aat aca gca	288
Thr Gly Val Leu Ser Asn Glu Leu Asp Leu Asp Glu Leu Asn Thr Ala	
85 90 95	
gag ttg tta tat aac gca agt gac ttg agc tac aag aag gga acg tcc	336
Glu Leu Leu Tyr Asn Ala Ser Asp Leu Ser Tyr Lys Lys Gly Thr Ser	
100 105 110	
att ggc gat agt gct cga ttg gct tat tat tta aga gct cat tat ata	384
Ile Gly Asp Ser Ala Arg Leu Ala Tyr Tyr Leu Arg Ala His Tyr Ile	
115 120 125	
cta aac att gtt gga tac tta gtt tcg cat aaa cgt tta gat atc atc	432
Leu Asn Ile Val Gly Tyr Leu Val Ser His Lys Arg Leu Asp Ile Ile	
130 135 140	
act aac aac aac caa gtg ttg ttt gac aat att ttg aaa agt ttc agc	480
Thr Asn Asn Asn Gln Val Leu Phe Asp Asn Ile Leu Lys Ser Phe Ser	
145 150 155 160	
aag att tat act ttg agt ggt aaa tta aat gac atg att gac aag caa	528
Lys Ile Tyr Thr Leu Ser Gly Lys Leu Asn Asp Met Ile Asp Lys Gln	
165 170 175	
aaa gtt acc ggc gac atc aac aat ctt gca ttt atc aat tgt atc aat	576
Lys Val Thr Gly Asp Ile Asn Asn Leu Ala Phe Ile Asn Cys Ile Asn	
180 185 190	
tat tcc aga agt cag ttg ttt aat gca cac gag tta ttg gga caa gtt	624
Tyr Ser Arg Ser Gln Leu Phe Asn Ala His Glu Leu Leu Gly Gln Val	
195 200 205	
gta ttt gga tta gcg gat aat tat tat gag agt tat ggc aca cta aac	672
Val Phe Gly Leu Ala Asp Asn Tyr Tyr Glu Ser Tyr Gly Thr Leu Asn	
210 215 220	
aac tat aat tcc tta gtg gag ttt ata ctg aaa aat atc agc gat gaa	720
Asn Tyr Asn Ser Leu Val Glu Phe Ile Leu Lys Asn Ile Ser Asp Glu	
225 230 235 240	
gat gtt ttt gtt atc cat ttt tta cca tcc act tta caa ttg ttc aag	768
Asp Val Phe Val Ile His Phe Leu Pro Ser Thr Leu Gln Leu Phe Lys	
245 250 255	
aaa tta ctt caa cta ggt gag gaa tct tta gtc gat cag ttt tac aag	816
Lys Leu Leu Gln Leu Gly Glu Glu Ser Leu Val Asp Gln Phe Tyr Lys	
260 265 270	
act ata acc tct tcc ata cta aaa gat tat gaa gcc aac aat ttt tcc	864
Thr Ile Thr Ser Ser Ile Leu Lys Asp Tyr Glu Ala Asn Asn Phe Ser	
275 280 285	
aaa agt gaa gat att gac ttg tca aaa tca aaa ttg tct ggc ttt gaa	912
Lys Ser Glu Asp Ile Asp Leu Ser Lys Ser Lys Leu Ser Gly Phe Glu	
290 295 300	
ata gtc aca agc ttt att ttt cta act gag ttt att cca tgg tgc aag	960

Ile Val Thr Ser Phe	Ile Phe Leu Thr Glu Phe	Ile Pro Trp Cys Lys	
305	310	315	320
cag ctg tca agt aga acc gcg aaa tac gat ttc aaa gat gat ata tta			1008
Gln Leu Ser Ser Arg Thr Ala Lys Tyr Asp Phe Lys Asp Asp Ile Leu			
	325	330	335
aag tat atg gaa ttc ttg ata agt tat gga gtt atg gaa cga tta tta			1056
Lys Tyr Met Glu Phe Leu Ile Ser Tyr Gly Val Met Glu Arg Leu Leu			
	340	345	350
tca tac tgt tct gaa acc agc aat gca aaa act cag caa gtg tac gac			1104
Ser Tyr Cys Ser Glu Thr Ser Asn Ala Lys Thr Gln Gln Val Tyr Asp			
	355	360	365
tgg tca aac atg tac gat ttc aga gca ttg ctt caa aag aat ttc cca			1152
Trp Ser Asn Met Tyr Asp Phe Arg Ala Leu Leu Gln Lys Asn Phe Pro			
	370	375	380
cga ctt aca cca gca aaa ttt cat tat cct ggc aat caa gaa ttg ttg			1200
Arg Leu Thr Pro Ala Lys Phe His Tyr Pro Gly Asn Gln Glu Leu Leu			
	385	390	400
aat gca gtt aga ccg gga tat gaa aat ata tcc aaa ttg att gac att			1248
Asn Ala Val Arg Pro Gly Tyr Glu Asn Ile Ser Lys Leu Ile Asp Ile			
	405	410	415
tcc ttt ttg acg tta gat cca tcc ctt aat gag acg ttg gtt tca cct			1296
Ser Phe Leu Thr Leu Asp Pro Ser Leu Asn Glu Thr Leu Val Ser Pro			
	420	425	430
ttt ttc cag agc ttt ttc agt gtg ttt ata tct aat gcc gca gtt gtt			1344
Phe Phe Gln Ser Phe Phe Ser Val Phe Ile Ser Asn Ala Ala Val Val			
	435	440	445
atg acc tct tta agg gac tca gag gaa gat ttt gtt tta tcc tcc ttg			1392
Met Thr Ser Leu Arg Asp Ser Glu Glu Asp Phe Val Leu Ser Ser Leu			
	450	455	460
aat gaa agt gac gaa gag gaa gaa gaa gaa gaa agc gac agc gac gaa			1440
Asn Glu Ser Asp Glu Glu Glu Glu Glu Glu Glu Ser Asp Ser Asp Glu			
	465	470	475
gat tct tcc acc cca aaa aac aaa gaa aaa tca gct ggg tta gac ctt			1488
Asp Ser Ser Thr Pro Lys Asn Lys Glu Lys Ser Ala Gly Leu Asp Leu			
	485	490	495
gac aag att gcc cag cgt gct gaa tta gaa agg ttc tac ttg gct ttc			1536
Asp Lys Ile Ala Gln Arg Ala Glu Leu Glu Arg Phe Tyr Leu Ala Phe			
	500	505	510
gcg tac acc tac aac aat cga cct gaa ttg tgt gcg tta ttt tgg ggg			1584
Ala Tyr Thr Tyr Asn Asn Arg Pro Glu Leu Cys Ala Leu Phe Trp Gly			
	515	520	525
aac gag cag gta act cat gac att ata gga ttt att tcc tgg gga ctt			1632
Asn Glu Gln Val Thr His Asp Ile Ile Gly Phe Ile Ser Trp Gly Leu			

530	535	540	
gct aat aat acg tct ccg ttg atc act gca aca ttc tgc tta cta tta			1680
Ala Asn Asn Thr Ser Pro Leu Ile Thr Ala Thr Phe Cys Leu Leu Leu			
545	550	555	560
ggg tcg ttg gca tct gct ggt gca gag gca act tca agg ata tgg gag			1728
Gly Ser Leu Ala Ser Ala Gly Ala Glu Ala Thr Ser Arg Ile Trp Glu			
	565	570	575
att ctt gta cac aac aat aac aac gca agt acg aga aaa aat gat ttt			1776
Ile Leu Val His Asn Asn Asn Asn Ala Ser Thr Arg Lys Asn Asp Phe			
	580	585	590
tca aag gta tcc gtt gac tcc ctt tat gat tcg ttg aaa tat tac att			1824
Ser Lys Val Ser Val Asp Ser Leu Tyr Asp Ser Leu Lys Tyr Tyr Ile			
	595	600	605
gac tct tta aat gaa agc ttt gaa caa gat tta aat gcc caa ttg atg			1872
Asp Ser Leu Asn Glu Ser Phe Glu Gln Asp Leu Asn Ala Gln Leu Met			
	610	615	620
ttg aat cag aag aaa caa gat ttt ctc ttc agc acc aca aca agc aaa			1920
Leu Asn Gln Lys Lys Gln Asp Phe Leu Phe Ser Thr Thr Thr Ser Lys			
	625	630	635
cag gac ctt gat gat tct ggc gag aat aga att gtt ata gag ttg gcc			1968
Gln Asp Leu Asp Asp Ser Gly Glu Asn Arg Ile Val Ile Glu Leu Ala			
	645	650	655
gag gat tca ctt gtc ctc att tca ggg ttt att caa tta ctt tct gca			2016
Glu Asp Ser Leu Val Leu Ile Ser Gly Phe Ile Gln Leu Leu Ser Ala			
	660	665	670
att gtg aag aat ttg aac act aag aat gaa aga agc aaa gaa atc aaa			2064
Ile Val Lys Asn Leu Asn Thr Lys Asn Glu Arg Ser Lys Glu Ile Lys			
	675	680	685
tcc gtg gta tac act aga ttc tca cca atc att aaa ggg ttt tta aaa			2112
Ser Val Val Tyr Thr Arg Phe Ser Pro Ile Ile Lys Gly Phe Leu Lys			
	690	695	700
ttc gat aat ttg atc aat ggt agc agg ttc ctt caa gtt gat gct agc			2160
Phe Asp Asn Leu Ile Asn Gly Ser Arg Phe Leu Gln Val Asp Ala Ser			
	705	710	715
att caa agc aca aac aac ccc aaa ttt att gat ttg cca aat gtt ttc			2208
Ile Gln Ser Thr Asn Asn Pro Lys Phe Ile Asp Leu Pro Asn Val Phe			
	725	730	735
gtc agt gat gac tcg aga att ata ttg acg aac ctc att cta acc ttt			2256
Val Ser Asp Asp Ser Arg Ile Ile Leu Thr Asn Leu Ile Leu Thr Phe			
	740	745	750
tta ggc gat ttt gtt acc aac gat agt gat ccg tat att aga tat gag			2304
Leu Gly Asp Phe Val Thr Asn Asp Ser Asp Pro Tyr Ile Arg Tyr Glu			
	755	760	765

att tgg cgt tta gtc gat cga tgg atg tac cag ggg ttg cat agt ttg	2352
Ile Trp Arg Leu Val Asp Arg Trp Met Tyr Gln Gly Leu His Ser Leu	
770 775 780	
cca gaa gac aag aaa gat gat gct ttt aga cat att aag aga aag tat	2400
Pro Glu Asp Lys Lys Asp Asp Ala Phe Arg His Ile Lys Arg Lys Tyr	
785 790 795 800	
aac agt aag aaa aat gtt ccc atc aat caa gca ttt tca aca aac cta	2448
Asn Ser Lys Lys Asn Val Pro Ile Asn Gln Ala Phe Ser Thr Asn Leu	
805 810 815	
act cat ctt agt caa att ggg aat ttc act gtc ttg gtg aaa aaa ttg	2496
Thr His Leu Ser Gln Ile Gly Asn Phe Thr Val Leu Val Lys Lys Leu	
820 825 830	
tta acc cca tat gca gat agt aat gaa gca ttc acc aag tac tcg ttg	2544
Leu Thr Pro Tyr Ala Asp Ser Asn Glu Ala Phe Thr Lys Tyr Ser Leu	
835 840 845	
ttg tat cct tgt gac tta gga tta ggg tat aga ttc aac aac caa ctt	2592
Leu Tyr Pro Cys Asp Leu Gly Leu Gly Tyr Arg Phe Asn Asn Gln Leu	
850 855 860	
gga att tgg cca tac att gaa ttt tta atg caa aat gtg ttt gca aat	2640
Gly Ile Trp Pro Tyr Ile Glu Phe Leu Met Gln Asn Val Phe Ala Asn	
865 870 875 880	
tct ggt act att gct aat aaa cga gat agg gtc aac ttg caa ctt aat	2688
Ser Gly Thr Ile Ala Asn Lys Arg Asp Arg Val Asn Leu Gln Leu Asn	
885 890 895	
ttg cta gaa tta ttt agc aat gca tta cag gga gtt gac tgg aag ttt	2736
Leu Leu Glu Leu Phe Ser Asn Ala Leu Gln Gly Val Asp Trp Lys Phe	
900 905 910	
ctt att gat gtg gca ccg aaa att att cgt gac ttg aaa aat ttt aat	2784
Leu Ile Asp Val Ala Pro Lys Ile Ile Arg Asp Leu Lys Asn Phe Asn	
915 920 925	
ggg ata ttt gac tcg ctt att cct ggt gtt caa ttg gac ttt gaa gtg	2832
Gly Ile Phe Asp Ser Leu Ile Pro Gly Val Gln Leu Asp Phe Glu Val	
930 935 940	
ttt gtc aaa ttg cat cat tca gtt gct gtg att aac tat cta ttt gaa	2880
Phe Val Lys Leu His His Ser Val Ala Val Ile Asn Tyr Leu Phe Glu	
945 950 955 960	
aac agg aca ttt tct gcc ttg ttt aag ctt gtt aat att gga gtt gat	2928
Asn Arg Thr Phe Ser Ala Leu Phe Lys Leu Val Asn Ile Gly Val Asp	
965 970 975	
tct gtg aat gaa tca ggt gaa tcg gcg gaa ttg gtg tca cat gcc ctt	2976
Ser Val Asn Glu Ser Gly Glu Ser Ala Glu Leu Val Ser His Ala Leu	
980 985 990	

ggg ttg att aat tct ttg ttg aga gtt caa aat tct ttt ata aac aag 3024
 Gly Leu Ile Asn Ser Leu Leu Arg Val Gln Asn Ser Phe Ile Asn Lys
 995 1000 1005

ttg tta cca ata ttg cga aac aaa gat acg cag caa caa tta cat cgt 3072
 Leu Leu Pro Ile Leu Arg Asn Lys Asp Thr Gln Gln Gln Leu His Arg
 1010 1015 1020

ggg aca gcc att ggg att ggt act tct atg agt ctt gcg tta gca acc 3120
 Gly Thr Ala Ile Gly Ile Gly Thr Ser Met Ser Leu Ala Leu Ala Thr
 1025 1030 1035 1040

cct aga acc ata ttt gat tgt ata tac tat cca aag aat ttg gga aca 3168
 Pro Arg Thr Ile Phe Asp Cys Ile Tyr Tyr Pro Lys Asn Leu Gly Thr
 1045 1050 1055

cat ggt gtt gct gat ttt tac gaa gtg ata ttg ttc cac tta tct gca 3216
 His Gly Val Ala Asp Phe Tyr Glu Val Ile Leu Phe His Leu Ser Ala
 1060 1065 1070

gtt gtc caa ttt gcc ctt tat gtc agt tgt gaa aat act att tcc aac 3264
 Val Val Gln Phe Ala Leu Tyr Val Ser Cys Glu Asn Thr Ile Ser Asn
 1075 1080 1085

aaa gca att tcc ata ttg aaa gga gta agc caa tcc aag ttt ttt gtt 3312
 Lys Ala Ile Ser Ile Leu Lys Gly Val Ser Gln Ser Lys Phe Phe Val
 1090 1095 1100

acc aga gtt tca agc tct gct gat ccc tta ctc aac aac gat aga ttg 3360
 Thr Arg Val Ser Ser Ser Ala Asp Pro Leu Leu Asn Asn Asp Arg Leu
 1105 1110 1115 1120

att acc aca ttt gaa aac atc gac gag tca ata aaa atc aag ttt gct 3408
 Ile Thr Thr Phe Glu Asn Ile Asp Glu Ser Ile Lys Ile Lys Phe Ala
 1125 1130 1135

ttc att gac aag ttt gaa gaa ctc gag gac tct ttg aat atg aaa tat 3456
 Phe Ile Asp Lys Phe Glu Glu Leu Glu Asp Ser Leu Asn Met Lys Tyr
 1140 1145 1150

gag ata ttg gat ttt gtt ttg ggc aat ctc aat caa ttt gat ggc aaa 3504
 Glu Ile Leu Asp Phe Val Leu Gly Asn Leu Asn Gln Phe Asp Gly Lys
 1155 1160 1165

gtg gct act act gcc cac ttt ttg ttg gga tac aaa gtg aaa ggc gat 3552
 Val Ala Thr Thr Ala His Phe Leu Leu Gly Tyr Lys Val Lys Gly Asp
 1170 1175 1180

aca tta gac ttg gta cag aca aac gat caa aac aca tta cta aaa tct 3600
 Thr Leu Asp Leu Val Gln Thr Asn Asp Gln Asn Thr Leu Leu Lys Ser
 1185 1190 1195 1200

ttc tta aat aca ttg agc att agt ctt gat ttg att tct gaa att gat 3648
 Phe Leu Asn Thr Leu Ser Ile Ser Leu Asp Leu Ile Ser Glu Ile Asp
 1205 1210 1215

tac aat aat ggt aat aac cat att att gat gtt ggt cca gcc aag ctt 3696

Tyr Asn Asn Gly Asn Asn His Ile Ile Asp Val Gly Pro Ala Lys Leu	
1220 1225 1230	
tcg tcg ttg att tta cag att ctt atc aag ttg tgc caa gat cca att	3744
Ser Ser Leu Ile Leu Gln Ile Leu Ile Lys Leu Cys Gln Asp Pro Ile	
1235 1240 1245	
tcg tcg tca ata aca ttg aat caa tta cgt gaa tat gaa gaa ttg ttt	3792
Ser Ser Ser Ile Thr Leu Asn Gln Leu Arg Glu Tyr Glu Glu Leu Phe	
1250 1255 1260	
gaa aaa ttg gtt aac tgt caa cct aaa ctt gat ttg aat acc gtt tgg	3840
Glu Lys Leu Val Asn Cys Gln Pro Lys Leu Asp Leu Asn Thr Val Trp	
1265 1270 1275 1280	
tgt ggt aac cag ttt gat ggg gat ttg cag att gat gct agc aat gta	3888
Cys Gly Asn Gln Phe Asp Gly Asp Leu Gln Ile Asp Ala Ser Asn Val	
1285 1290 1295	
ttt gtt gac aac caa gca agc acc cag gct ttc ttt tcc ttt att aac	3936
Phe Val Asp Asn Gln Ala Ser Thr Gln Ala Phe Phe Ser Phe Ile Asn	
1300 1305 1310	
cag aga aac tta att ttg cag tat ttg tca ttg gaa ttc cat agt gtc	3984
Gln Arg Asn Leu Ile Leu Gln Tyr Leu Ser Leu Glu Phe His Ser Val	
1315 1320 1325	
aaa tca aga act aag cgg gag tat tat tct aaa gtg ttg acc aac gac	4032
Lys Ser Arg Thr Lys Arg Glu Tyr Tyr Ser Lys Val Leu Thr Asn Asp	
1330 1335 1340	
aag gaa ttt gtt aat cgt aca cct aag gtg ttg aca ttt tta aac att	4080
Lys Glu Phe Val Asn Arg Thr Pro Lys Val Leu Thr Phe Leu Asn Ile	
1345 1350 1355 1360	
cta aat tat tca ttc aag aac ttt gaa gtg cag aaa tac gaa tgg ctt	4128
Leu Asn Tyr Ser Phe Lys Asn Phe Glu Val Gln Lys Tyr Glu Trp Leu	
1365 1370 1375	
gac caa aaa ttt aac gtg tcg ttg tta ttg gca gaa gta aac gct caa	4176
Asp Gln Lys Phe Asn Val Ser Leu Leu Leu Ala Glu Val Asn Ala Gln	
1380 1385 1390	
aag aat ggt aca tta gat ttt tct gtt tta aca aag gtt ttc cgt ctt	4224
Lys Asn Gly Thr Leu Asp Phe Ser Val Leu Thr Lys Val Phe Arg Leu	
1395 1400 1405	
ttg tgc caa acg tca aac tta ata aca ccc gag tca aag caa ttg ttt	4272
Leu Cys Gln Thr Ser Asn Leu Ile Thr Pro Glu Ser Lys Gln Leu Phe	
1410 1415 1420	
gcc gaa gaa att atg gtt gaa gga agt aag att tct gac ttt gtc aca	4320
Ala Glu Glu Ile Met Val Glu Gly Ser Lys Ile Ser Asp Phe Val Thr	
1425 1430 1435 1440	
aag tac ctg gtg tcg acc gac ttg aag gat gtg cag ttg aaa tgc tta	4368
Lys Tyr Leu Val Ser Thr Asp Leu Lys Asp Val Gln Leu Lys Cys Leu	

1445	1450	1455	
cat tca tgg tgt caa ttg ata gag att ttg gtt act gac agt gga atc			4416
His Ser Trp Cys Gln Leu Ile Glu Ile Leu Val Thr Asp Ser Gly Ile			
1460	1465	1470	
aat tcg ctg aat ttc atc ttg gaa gtg ttg caa gtt att att ccc aaa			4464
Asn Ser Leu Asn Phe Ile Leu Glu Val Leu Gln Val Ile Ile Pro Lys			
1475	1480	1485	
atc aat gac tat ttt gat gtg gac ata ctg ttt tct gaa gaa atg gtt			4512
Ile Asn Asp Tyr Phe Asp Val Asp Ile Leu Phe Ser Glu Glu Met Val			
1490	1495	1500	
tca tta tgt gtt tta ttg ttt gat ctt tat gat cag ctg act ctt gcg			4560
Ser Leu Cys Val Leu Leu Phe Asp Leu Tyr Asp Gln Leu Thr Leu Ala			
1505	1510	1515	1520
gac aga aaa ggt gaa gat ttt gca ctt gga att gag aga ttg atc ccc			4608
Asp Arg Lys Gly Glu Asp Phe Ala Leu Gly Ile Glu Arg Leu Ile Pro			
1525	1530	1535	
tta ttt cag act tgt att gca ggt att ctt aat tct aac tca aca ccc			4656
Leu Phe Gln Thr Cys Ile Ala Gly Ile Leu Asn Ser Asn Ser Thr Pro			
1540	1545	1550	
agc tta cgc tca gac ttg tat gta gtt ggc aac aag ttt ttg tta aaa			4704
Ser Leu Arg Ser Asp Leu Tyr Val Val Gly Asn Lys Phe Leu Leu Lys			
1555	1560	1565	
tgt ttt gag aga gag tcg ttt ttg aaa caa gtg atg cat atc atc aag			4752
Cys Phe Glu Arg Glu Ser Phe Leu Lys Gln Val Met His Ile Ile Lys			
1570	1575	1580	
tcg gta gat aaa aag ttt ttc cag gtg att tgt aat gac gct atc tac			4800
Ser Val Asp Lys Lys Phe Phe Gln Val Ile Cys Asn Asp Ala Ile Tyr			
1585	1590	1595	1600
tca gag ggt cca tct aga atc act tct act tta ttc ctc gag tca tta			4848
Ser Glu Gly Pro Ser Arg Ile Thr Ser Thr Leu Phe Leu Glu Ser Leu			
1605	1610	1615	
gtt cac tta ggg act ttg gtc aag gtt gat ttt att ttg aat gcg ttg			4896
Val His Leu Gly Thr Leu Val Lys Val Asp Phe Ile Leu Asn Ala Leu			
1620	1625	1630	
atc aaa aat aac gca ttg ctg ttg cta gtc agg tca gtt aag cgg act			4944
Ile Lys Asn Asn Ala Leu Leu Leu Leu Val Arg Ser Val Lys Arg Thr			
1635	1640	1645	
gat gcc atg atc aaa ttg tgc cag gaa aaa aat tca gga gtg act tta			4992
Asp Ala Met Ile Lys Leu Cys Gln Glu Lys Asn Ser Gly Val Thr Leu			
1650	1655	1660	
gat cat ttc ata ttt gac ttg atg gca ttc aaa gca acg cta tat ttt			5040
Asp His Phe Ile Phe Asp Leu Met Ala Phe Lys Ala Thr Leu Tyr Phe			
1665	1670	1675	1680

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ttt gtt aga gtg gcc aaa tcg aaa aac ggg gca ttg cag ttg att caa 5088
 Phe Val Arg Val Ala Lys Ser Lys Asn Gly Ala Leu Gln Leu Ile Gln
 1685 1690 1695

aat gaa ttg ttt tca att ttg cat cag tcg aag ttt ttg cag att gat 5136
 Asn Glu Leu Phe Ser Ile Leu His Gln Ser Lys Phe Leu Gln Ile Asp
 1700 1705 1710

cca gat att ggt tta agt tta cga att gaa gaa gtt caa gat cac aag 5184
 Pro Asp Ile Gly Leu Ser Leu Arg Ile Glu Glu Val Gln Asp His Lys
 1715 1720 1725

act gtc aat gta aat gtt ttg cta gat act cca ctt tcg ata act gac 5232
 Thr Val Asn Val Asn Val Leu Leu Asp Thr Pro Leu Ser Ile Thr Asp
 1730 1735 1740

ttg gtg gat cca tac aag ttg cga agt gaa aac act ata tca tat ttt 5280
 Leu Val Asp Pro Tyr Lys Leu Arg Ser Glu Asn Thr Ile Ser Tyr Phe
 1745 1750 1755 1760

gag ttc ctt gta cca ata ttt cag cta ctt aca aca gtg tta ttg tca 5328
 Glu Phe Leu Val Pro Ile Phe Gln Leu Leu Thr Thr Val Leu Leu Ser
 1765 1770 1775

atg gga cca aat tat caa cct gca att att caa act aga gaa ctt atg 5376
 Met Gly Pro Asn Tyr Gln Pro Ala Ile Ile Gln Thr Arg Glu Leu Met
 1780 1785 1790

aag agt gta aat cga ttg gtg gta ggt gtt atg aaa aga gat ttc ttg 5424
 Lys Ser Val Asn Arg Leu Val Val Gly Val Met Lys Arg Asp Phe Leu
 1795 1800 1805

gta gag acc aaa caa att ggt caa ggg ttg tac aag gaa gag agt cac 5472
 Val Glu Thr Lys Gln Ile Gly Gln Gly Leu Tyr Lys Glu Glu Ser His
 1810 1815 1820

gag ttg gta tcg ttg aaa gaa ttg gtg aag ttg ttt att ttg att gat 5520
 Glu Leu Val Ser Leu Lys Glu Leu Val Lys Leu Phe Ile Leu Ile Asp
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 Ser Leu Ala His Tyr Ser Val
 1845

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<212> PRT

<213> Candida albicans

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Thr Ser Ile Lys Asn Asp Leu Ala Asn Val Leu Ile Thr Pro Val Pro
 35 40 45
 Leu Asp Gln Ser Arg Ser Lys Leu Gly Asp Ala Ser Lys Pro Val Ala
 50 55 60
 Leu Pro Ser Gly Asp Glu Val Lys Leu Asn Gln Ala Ser Ile Glu Ile
 65 70 75 80
 Thr Gly Val Leu Ser Asn Glu Leu Asp Leu Asp Glu Leu Asn Thr Ala
 85 90 95
 Glu Leu Leu Tyr Asn Ala Ser Asp Leu Ser Tyr Lys Lys Gly Thr Ser
 100 105 110
 Ile Gly Asp Ser Ala Arg Leu Ala Tyr Tyr Leu Arg Ala His Tyr Ile
 115 120 125
 Leu Asn Ile Val Gly Tyr Leu Val Ser His Lys Arg Leu Asp Ile Ile
 130 135 140
 Thr Asn Asn Asn Gln Val Leu Phe Asp Asn Ile Leu Lys Ser Phe Ser
 145 150 155 160
 Lys Ile Tyr Thr Leu Ser Gly Lys Leu Asn Asp Met Ile Asp Lys Gln
 165 170 175
 Lys Val Thr Gly Asp Ile Asn Asn Leu Ala Phe Ile Asn Cys Ile Asn
 180 185 190
 Tyr Ser Arg Ser Gln Leu Phe Asn Ala His Glu Leu Leu Gly Gln Val
 195 200 205
 Val Phe Gly Leu Ala Asp Asn Tyr Tyr Glu Ser Tyr Gly Thr Leu Asn
 210 215 220
 Asn Tyr Asn Ser Leu Val Glu Phe Ile Leu Lys Asn Ile Ser Asp Glu
 225 230 235 240
 Asp Val Phe Val Ile His Phe Leu Pro Ser Thr Leu Gln Leu Phe Lys
 245 250 255
 Lys Leu Leu Gln Leu Gly Glu Glu Ser Leu Val Asp Gln Phe Tyr Lys
 260 265 270
 Thr Ile Thr Ser Ser Ile Leu Lys Asp Tyr Glu Ala Asn Asn Phe Ser
 275 280 285
 Lys Ser Glu Asp Ile Asp Leu Ser Lys Ser Lys Leu Ser Gly Phe Glu
 290 295 300
 Ile Val Thr Ser Phe Ile Phe Leu Thr Glu Phe Ile Pro Trp Cys Lys
 305 310 315 320
 Gln Leu Ser Ser Arg Thr Ala Lys Tyr Asp Phe Lys Asp Asp Ile Leu
 325 330 335

Lys Tyr Met Glu Phe Leu Ile Ser Tyr Gly Val Met Glu Arg Leu Leu
 340 345 350
 Ser Tyr Cys Ser Glu Thr Ser Asn Ala Lys Thr Gln Gln Val Tyr Asp
 355 360 365
 Trp Ser Asn Met Tyr Asp Phe Arg Ala Leu Leu Gln Lys Asn Phe Pro
 370 375 380
 Arg Leu Thr Pro Ala Lys Phe His Tyr Pro Gly Asn Gln Glu Leu Leu
 385 390 395 400
 Asn Ala Val Arg Pro Gly Tyr Glu Asn Ile Ser Lys Leu Ile Asp Ile
 405 410 415
 Ser Phe Leu Thr Leu Asp Pro Ser Leu Asn Glu Thr Leu Val Ser Pro
 420 425 430
 Phe Phe Gln Ser Phe Phe Ser Val Phe Ile Ser Asn Ala Ala Val Val
 435 440 445
 Met Thr Ser Leu Arg Asp Ser Glu Glu Asp Phe Val Leu Ser Ser Leu
 450 455 460
 Asn Glu Ser Asp Glu Glu Glu Glu Glu Glu Ser Asp Ser Asp Glu
 465 470 475 480
 Asp Ser Ser Thr Pro Lys Asn Lys Glu Lys Ser Ala Gly Leu Asp Leu
 485 490 495
 Asp Lys Ile Ala Gln Arg Ala Glu Leu Glu Arg Phe Tyr Leu Ala Phe
 500 505 510
 Ala Tyr Thr Tyr Asn Asn Arg Pro Glu Leu Cys Ala Leu Phe Trp Gly
 515 520 525
 Asn Glu Gln Val Thr His Asp Ile Ile Gly Phe Ile Ser Trp Gly Leu
 530 535 540
 Ala Asn Asn Thr Ser Pro Leu Ile Thr Ala Thr Phe Cys Leu Leu Leu
 545 550 555 560
 Gly Ser Leu Ala Ser Ala Gly Ala Glu Ala Thr Ser Arg Ile Trp Glu
 565 570 575
 Ile Leu Val His Asn Asn Asn Asn Ala Ser Thr Arg Lys Asn Asp Phe
 580 585 590
 Ser Lys Val Ser Val Asp Ser Leu Tyr Asp Ser Leu Lys Tyr Tyr Ile
 595 600 605
 Asp Ser Leu Asn Glu Ser Phe Glu Gln Asp Leu Asn Ala Gln Leu Met
 610 615 620
 Leu Asn Gln Lys Lys Gln Asp Phe Leu Phe Ser Thr Thr Thr Ser Lys
 625 630 635 640

Gln Asp Leu Asp Asp Ser Gly Glu Asn Arg Ile Val Ile Glu Leu Ala
 645 650 655
 Glu Asp Ser Leu Val Leu Ile Ser Gly Phe Ile Gln Leu Leu Ser Ala
 660 665 670
 Ile Val Lys Asn Leu Asn Thr Lys Asn Glu Arg Ser Lys Glu Ile Lys
 675 680 685
 Ser Val Val Tyr Thr Arg Phe Ser Pro Ile Ile Lys Gly Phe Leu Lys
 690 695 700
 Phe Asp Asn Leu Ile Asn Gly Ser Arg Phe Leu Gln Val Asp Ala Ser
 705 710 715 720
 Ile Gln Ser Thr Asn Asn Pro Lys Phe Ile Asp Leu Pro Asn Val Phe
 725 730 735
 Val Ser Asp Asp Ser Arg Ile Ile Leu Thr Asn Leu Ile Leu Thr Phe
 740 745 750
 Leu Gly Asp Phe Val Thr Asn Asp Ser Asp Pro Tyr Ile Arg Tyr Glu
 755 760 765
 Ile Trp Arg Leu Val Asp Arg Trp Met Tyr Gln Gly Leu His Ser Leu
 770 775 780
 Pro Glu Asp Lys Lys Asp Asp Ala Phe Arg His Ile Lys Arg Lys Tyr
 785 790 795 800
 Asn Ser Lys Lys Asn Val Pro Ile Asn Gln Ala Phe Ser Thr Asn Leu
 805 810 815
 Thr His Leu Ser Gln Ile Gly Asn Phe Thr Val Leu Val Lys Lys Leu
 820 825 830
 Leu Thr Pro Tyr Ala Asp Ser Asn Glu Ala Phe Thr Lys Tyr Ser Leu
 835 840 845
 Leu Tyr Pro Cys Asp Leu Gly Leu Gly Tyr Arg Phe Asn Asn Gln Leu
 850 855 860
 Gly Ile Trp Pro Tyr Ile Glu Phe Leu Met Gln Asn Val Phe Ala Asn
 865 870 875 880
 Ser Gly Thr Ile Ala Asn Lys Arg Asp Arg Val Asn Leu Gln Leu Asn
 885 890 895
 Leu Leu Glu Leu Phe Ser Asn Ala Leu Gln Gly Val Asp Trp Lys Phe
 900 905 910
 Leu Ile Asp Val Ala Pro Lys Ile Ile Arg Asp Leu Lys Asn Phe Asn
 915 920 925
 Gly Ile Phe Asp Ser Leu Ile Pro Gly Val Gln Leu Asp Phe Glu Val
 930 935 940

Phe Val Lys Leu His His Ser Val Ala Val Ile Asn Tyr Leu Phe Glu
 945 950 955 960
 Asn Arg Thr Phe Ser Ala Leu Phe Lys Leu Val Asn Ile Gly Val Asp
 965 970 975
 Ser Val Asn Glu Ser Gly Glu Ser Ala Glu Leu Val Ser His Ala Leu
 980 985 990
 Gly Leu Ile Asn Ser Leu Leu Arg Val Gln Asn Ser Phe Ile Asn Lys
 995 1000 1005
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 Gly Thr Ala Ile Gly Ile Gly Thr Ser Met Ser Leu Ala Leu Ala Thr
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 Pro Arg Thr Ile Phe Asp Cys Ile Tyr Tyr Pro Lys Asn Leu Gly Thr
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 His Gly Val Ala Asp Phe Tyr Glu Val Ile Leu Phe His Leu Ser Ala
 1060 1065 1070
 Val Val Gln Phe Ala Leu Tyr Val Ser Cys Glu Asn Thr Ile Ser Asn
 1075 1080 1085
 Lys Ala Ile Ser Ile Leu Lys Gly Val Ser Gln Ser Lys Phe Phe Val
 1090 1095 1100
 Thr Arg Val Ser Ser Ser Ala Asp Pro Leu Leu Asn Asn Asp Arg Leu
 105 1110 1115 1120
 Ile Thr Thr Phe Glu Asn Ile Asp Glu Ser Ile Lys Ile Lys Phe Ala
 1125 1130 1135
 Phe Ile Asp Lys Phe Glu Glu Leu Glu Asp Ser Leu Asn Met Lys Tyr
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 Glu Ile Leu Asp Phe Val Leu Gly Asn Leu Asn Gln Phe Asp Gly Lys
 1155 1160 1165
 Val Ala Thr Thr Ala His Phe Leu Leu Gly Tyr Lys Val Lys Gly Asp
 1170 1175 1180
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 Phe Leu Asn Thr Leu Ser Ile Ser Leu Asp Leu Ile Ser Glu Ile Asp
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 Tyr Asn Asn Gly Asn Asn His Ile Ile Asp Val Gly Pro Ala Lys Leu
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 Ser Ser Leu Ile Leu Gln Ile Leu Ile Lys Leu Cys Gln Asp Pro Ile
 1235 1240 1245

Ser Ser Ser Ile Thr Leu Asn Gln Leu Arg Glu Tyr Glu Glu Leu Phe
 1250 1255 1260

Glu Lys Leu Val Asn Cys Gln Pro Lys Leu Asp Leu Asn Thr Val Trp
 265 1270 1275 1280

Cys Gly Asn Gln Phe Asp Gly Asp Leu Gln Ile Asp Ala Ser Asn Val
 1285 1290 1295

Phe Val Asp Asn Gln Ala Ser Thr Gln Ala Phe Phe Ser Phe Ile Asn
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Gln Arg Asn Leu Ile Leu Gln Tyr Leu Ser Leu Glu Phe His Ser Val
 1315 1320 1325

Lys Ser Arg Thr Lys Arg Glu Tyr Tyr Ser Lys Val Leu Thr Asn Asp
 1330 1335 1340

Lys Glu Phe Val Asn Arg Thr Pro Lys Val Leu Thr Phe Leu Asn Ile
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Leu Asn Tyr Ser Phe Lys Asn Phe Glu Val Gln Lys Tyr Glu Trp Leu
 1365 1370 1375

Asp Gln Lys Phe Asn Val Ser Leu Leu Leu Ala Glu Val Asn Ala Gln
 1380 1385 1390

Lys Asn Gly Thr Leu Asp Phe Ser Val Leu Thr Lys Val Phe Arg Leu
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Leu Cys Gln Thr Ser Asn Leu Ile Thr Pro Glu Ser Lys Gln Leu Phe
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Ala Glu Glu Ile Met Val Glu Gly Ser Lys Ile Ser Asp Phe Val Thr
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Lys Tyr Leu Val Ser Thr Asp Leu Lys Asp Val Gln Leu Lys Cys Leu
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His Ser Trp Cys Gln Leu Ile Glu Ile Leu Val Thr Asp Ser Gly Ile
 1460 1465 1470

Asn Ser Leu Asn Phe Ile Leu Glu Val Leu Gln Val Ile Ile Pro Lys
 1475 1480 1485

Ile Asn Asp Tyr Phe Asp Val Asp Ile Leu Phe Ser Glu Glu Met Val
 1490 1495 1500

Ser Leu Cys Val Leu Leu Phe Asp Leu Tyr Asp Gln Leu Thr Leu Ala
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Asp Arg Lys Gly Glu Asp Phe Ala Leu Gly Ile Glu Arg Leu Ile Pro
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Leu Phe Gln Thr Cys Ile Ala Gly Ile Leu Asn Ser Asn Ser Thr Pro
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Ser Leu Arg Ser Asp Leu Tyr Val Val Gly Asn Lys Phe Leu Leu Lys
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 Cys Phe Glu Arg Glu Ser Phe Leu Lys Gln Val Met His Ile Ile Lys
 1570 1575 1580
 Ser Val Asp Lys Lys Phe Phe Gln Val Ile Cys Asn Asp Ala Ile Tyr
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 Ser Glu Gly Pro Ser Arg Ile Thr Ser Thr Leu Phe Leu Glu Ser Leu
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 Val His Leu Gly Thr Leu Val Lys Val Asp Phe Ile Leu Asn Ala Leu
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 Ile Lys Asn Asn Ala Leu Leu Leu Leu Val Arg Ser Val Lys Arg Thr
 1635 1640 1645
 Asp Ala Met Ile Lys Leu Cys Gln Glu Lys Asn Ser Gly Val Thr Leu
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 Asp His Phe Ile Phe Asp Leu Met Ala Phe Lys Ala Thr Leu Tyr Phe
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 Phe Val Arg Val Ala Lys Ser Lys Asn Gly Ala Leu Gln Leu Ile Gln
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 Asn Glu Leu Phe Ser Ile Leu His Gln Ser Lys Phe Leu Gln Ile Asp
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 Pro Asp Ile Gly Leu Ser Leu Arg Ile Glu Glu Val Gln Asp His Lys
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 Thr Val Asn Val Asn Val Leu Leu Asp Thr Pro Leu Ser Ile Thr Asp
 1730 1735 1740
 Leu Val Asp Pro Tyr Lys Leu Arg Ser Glu Asn Thr Ile Ser Tyr Phe
 745 1750 1755 1760
 Glu Phe Leu Val Pro Ile Phe Gln Leu Leu Thr Thr Val Leu Leu Ser
 1765 1770 1775
 Met Gly Pro Asn Tyr Gln Pro Ala Ile Ile Gln Thr Arg Glu Leu Met
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 Lys Ser Val Asn Arg Leu Val Val Gly Val Met Lys Arg Asp Phe Leu
 1795 1800 1805
 Val Glu Thr Lys Gln Ile Gly Gln Gly Leu Tyr Lys Glu Glu Ser His
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 Ser Leu Ala His Tyr Ser Val
 1845

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 ttggtacaag gaactcaaaa tatgatatag tgttttctact tcgcaacttg tatggatcca 180
 ccaagtcagt tatcgaaagt ggagtatcta gcaaaacatt tacattgaca gtcttgtgat 240
 ctggaacttc ttcaaltcgt aaacttaaac caatatctgg atcaatctgc aaaaacttcg 300
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 aacaccaac cnaaaacac ccaacacctc catcttgtcc cgcttttctc tcacattttt 480
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 aacctacctc cctcaactcc tatttctctc ctcc 575

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 Trp Leu Pro Pro Pro His Pro Pro Asn Pro Thr Gly Ile Asp Ser Asp
 20 25 30
 ccg gct tta gca cca cat ggt gtt gaa caa gcc caa cag tta gct gcc 144
 Pro Ala Leu Ala Pro His Gly Val Glu Gln Ala Gln Gln Leu Ala Ala

35	40	45	
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Tyr Leu Thr Ser Leu Pro Thr His Glu Lys Pro Glu Phe Ile Ile Ala			
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tca cct ttt tat cgt tgt ata gaa acg tcg aga ccc att gcc gaa atg	240		
Ser Pro Phe Tyr Arg Cys Ile Glu Thr Ser Arg Pro Ile Ala Glu Met			
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Leu Asp Leu Lys Ile Ala Leu Glu Arg Gly Val Gly Glu Trp Phe Arg			
85 90 95			
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Lys Asn Arg Asp Thr Lys Pro Val Pro Gly Asp Tyr Thr Gln Leu Arg			
100 105 110			
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Thr Phe Phe Asp Lys Leu Leu Ile Asp Glu Asp Thr Trp Pro Arg Asp			
115 120 125			
aac tta aat gtt ata cct aat att gaa gga gaa gat tat gat gaa atc	432		
Asn Leu Asn Val Ile Pro Asn Ile Glu Gly Glu Asp Tyr Asp Glu Ile			
130 135 140			
tac gat cgt gcc aaa ttg ttt tgg aaa aag ttt att cct gaa ttt gaa	480		
Tyr Asp Arg Ala Lys Leu Phe Trp Lys Lys Phe Ile Pro Glu Phe Glu			
145 150 155 160			
aag aaa ttc ccc gaa att aaa aat gtg ttg ata gtt aca cat gca gca	528		
Lys Lys Phe Pro Glu Ile Lys Asn Val Leu Ile Val Thr His Ala Ala			
165 170 175			
acg aaa att gct tta gga tca gct tta tta cag tta aaa tca gtt act	576		
Thr Lys Ile Ala Leu Gly Ser Ala Leu Leu Gln Leu Lys Ser Val Thr			
180 185 190			
gat gtt ata gat gat aat caa act gtg tta cgt gct ggt gca tgt tca	624		
Asp Val Ile Asp Asp Asn Gln Thr Val Leu Arg Ala Gly Ala Cys Ser			
195 200 205			
tta tcc aaa ttt gtt aga gat ggc gaa gat aaa acc aat cat act att	672		
Leu Ser Lys Phe Val Arg Asp Gly Glu Asp Lys Thr Asn His Thr Ile			
210 215 220			
caa tgg aaa att gtc atg aat ggt aat tgt gaa ttc ttg aca cag ggt	720		
Gln Trp Lys Ile Val Met Asn Gly Asn Cys Glu Phe Leu Thr Gln Gly			
225 230 235 240			
gaa gaa atg aac tgg gat ttc cgt cgt ggt gtt gaa gcc ggg tca gct	768		
Glu Glu Met Asn Trp Asp Phe Arg Arg Gly Val Glu Ala Gly Ser Ala			
245 250 255			
gaa gat ata gcg caa aga aag gca gca gca gaa gca gaa gca aaa gca	816		
Glu Asp Ile Ala Gln Arg Lys Ala Ala Ala Glu Ala Glu Ala Lys Ala			
260 265 270			

ttg aag aaa aat gaa caa acc aaa tcc gat ggt ccc atc act gaa tct 864
Leu Lys Lys Asn Glu Gln Thr Lys Ser Asp Gly Pro Ile Thr Glu Ser
275 280 285

gcc act ggg gca gaa ata gat ggg aat gaa gat gaa ttt gaa gta cgt 912
Ala Thr Gly Ala Glu Ile Asp Gly Asn Glu Asp Glu Phe Glu Val Arg
290 295 300

aaa act tga 921
Lys Thr
305

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<210> 14
<211> 306
<212> PR'T
<213> Candida albicans
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<400> 14
Met Thr Ile Glu Thr Ile Tyr Ile Ala Arg His Gly Tyr Arg Ser Asn
1 5 10 15

Trp Leu Pro Pro Pro His Pro Pro Asn Pro Thr Gly Ile Asp Ser Asp
20 25 30

Pro Ala Leu Ala Pro His Gly Val Glu Gln Ala Gln Gln Leu Ala Ala
35 40 45

Tyr Leu Thr Ser Leu Pro Thr His Glu Lys Pro Glu Phe Ile Ile Ala
50 55 60

Ser Pro Phe Tyr Arg Cys Ile Glu Thr Ser Arg Pro Ile Ala Glu Met
65 70 75 80

Leu Asp Leu Lys Ile Ala Leu Glu Arg Gly Val Gly Glu Trp Phe Arg
85 90 95

Lys Asn Arg Asp Thr Lys Pro Val Pro Gly Asp Tyr Thr Gln Leu Arg
100 105 110

Thr Phe Phe Asp Lys Leu Leu Ile Asp Glu Asp Thr Trp Pro Arg Asp
115 120 125

Asn Leu Asn Val Ile Pro Asn Ile Glu Gly Glu Asp Tyr Asp Glu Ile
130 135 140

Tyr Asp Arg Ala Lys Leu Phe Trp Lys Lys Phe Ile Pro Glu Phe Glu
145 150 155 160

Lys Lys Phe Pro Glu Ile Lys Asn Val Leu Ile Val Thr His Ala Ala
165 170 175

Thr Lys Ile Ala Leu Gly Ser Ala Leu Leu Gln Leu Lys Ser Val Thr
180 185 190

Asp Val Ile Asp Asp Asn Gln Thr Val Leu Arg Ala Gly Ala Cys Ser

195

200

205

Leu Ser Lys Phe Val Arg Asp Gly Glu Asp Lys Thr Asn His Thr Ile
210 215 220

Gln Trp Lys Ile Val Met Asn Gly Asn Cys Glu Phe Leu Thr Gln Gly
225 230 235 240

Glu Glu Met Asn Trp Asp Phe Arg Arg Gly Val Glu Ala Gly Ser Ala
245 250 255

Glu Asp Ile Ala Gln Arg Lys Ala Ala Ala Glu Ala Glu Ala Lys Ala
260 265 270

Leu Lys Lys Asn Glu Gln Thr Lys Ser Asp Gly Pro Ile Thr Glu Ser
275 280 285

Ala Thr Gly Ala Glu Ile Asp Gly Asn Glu Asp Glu Phe Glu Val Arg
290 295 300

Lys Thr
305

<210> 15

<211> 1454

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Splice Variant

<220>

<221> CDS

<222> (1)..(1452)

<223> gene CaOR110 Splice Variant

<400> 15

atg acg att gaa act att tat atc gca aga cac ggt tat aga tcc aat 48
Met Thr Ile Glu Thr Ile Tyr Ile Ala Arg His Gly Tyr Arg Ser Asn
1 5 10 15

tgg tta cca cca cca cac cca cca aat cct act ggt att gac agt gac 96
Trp Leu Pro Pro Pro His Pro Pro Asn Pro Thr Gly Ile Asp Ser Asp
20 25 30

ccg gct tta gca cca cat ggt gtt gaa caa gcc caa cag tta gct gcc 144
Pro Ala Leu Ala Pro His Gly Val Glu Gln Ala Gln Gln Leu Ala Ala
35 40 45

tat ctt aca tca tta cct aca cat gaa aag cct gaa ttt att att gct 192
Tyr Leu Thr Ser Leu Pro Thr His Glu Lys Pro Glu Phe Ile Ile Ala
50 55 60

tca cct ttt tat cgt tgt ata gaa acg tcg aga ccc att gcc gaa atg 240
Ser Pro Phe Tyr Arg Cys Ile Glu Thr Ser Arg Pro Ile Ala Glu Met
65 70 75 80

ttg gac ttg aag att gct tta gaa aga gga gtt ggt gaa tgg ttt cgt	288
Leu Asp Leu Lys Ile Ala Leu Glu Arg Gly Val Gly Glu Trp Phe Arg	
85 90 95	
aaa aat aga gat acc aaa cca gtt ccc ggt gat tac aca caa ttg aga	336
Lys Asn Arg Asp Thr Lys Pro Val Pro Gly Asp Tyr Thr Gln Leu Arg	
100 105 110	
aca ttt ttc gat aaa tta ttg atc gat gaa gat act tgg cca aga gat	384
Thr Phe Phe Asp Lys Leu Leu Ile Asp Glu Asp Thr Trp Pro Arg Asp	
115 120 125	
aac tta aat gtt ata cct aat att gaa gga gaa gat tat gat gaa atc	432
Asn Leu Asn Val Ile Pro Asn Ile Glu Gly Glu Asp Tyr Asp Glu Ile	
130 135 140	
tac gat cgt gcc aaa ttg ttt tgg aaa aag ttt att cct gaa ttt gaa	480
Tyr Asp Arg Ala Lys Leu Phe Trp Lys Lys Phe Ile Pro Glu Phe Glu	
145 150 155 160	
aag aaa ttc ccc gaa att aaa aat gtg ttg ata gtt aca cat gca gca	528
Lys Lys Phe Pro Glu Ile Lys Asn Val Leu Ile Val Thr His Ala Ala	
165 170 175	
acg aaa att gct tta gga tca gct tta tta cag tta aaa tca gtt act	576
Thr Lys Ile Ala Leu Gly Ser Ala Leu Leu Gln Leu Lys Ser Val Thr	
180 185 190	
gat gtt ata gat gat aat caa act gtg tta cgt gct ggt gca tgt tca	624
Asp Val Ile Asp Asp Asn Gln Thr Val Leu Arg Ala Gly Ala Cys Ser	
195 200 205	
tta tcc aaa ttt gtt aga gat ggc gaa gat aaa acc aat cat act att	672
Leu Ser Lys Phe Val Arg Asp Gly Glu Asp Lys Thr Asn His Thr Ile	
210 215 220	
caa tgg aaa att gtc atg aat ggt aat tgt gaa ttc ttg aca cag ggt	720
Gln Trp Lys Ile Val Met Asn Gly Asn Cys Glu Phe Leu Thr Gln Gly	
225 230 235 240	
gaa gaa atg aac tgg gat ttc cgt cgt ggt gtt gaa gcc ggg tca gct	768
Glu Glu Met Asn Trp Asp Phe Arg Arg Gly Val Glu Ala Gly Ser Ala	
245 250 255	
gaa gat ata gcg caa aga aag gca gca gca gaa gca gaa gca aaa gca	816
Glu Asp Ile Ala Gln Arg Lys Ala Ala Ala Glu Ala Glu Ala Lys Ala	
260 265 270	
ttg aag aaa aat gaa caa acc aaa tcc gat ggt ccc atc act gaa tct	864
Leu Lys Lys Asn Glu Gln Thr Lys Ser Asp Gly Pro Ile Thr Glu Ser	
275 280 285	
gcc act ggg gca gaa ata gat ggg aat gaa gat gaa ttt gaa aca ttt	912
Ala Thr Gly Ala Glu Ile Asp Gly Asn Glu Asp Glu Phe Glu Thr Phe	
290 295 300	

tat gta acc atc gat ata cct tca att tcg aat aaa atc gac aat gaa	960
Tyr Val Thr Ile Asp Ile Pro Ser Ile Ser Asn Lys Ile Asp Asn Glu	
305 310 315 320	
gaa gaa cca cca tca agg aca ggt caa gct cca aaa ttc aaa aac aat	1008
Glu Glu Pro Pro Ser Arg Thr Gly Gln Ala Pro Lys Phe Lys Asn Asn	
325 330 335	
att atc aag cct tca gca caa ctc caa ttt act gat tta aaa gaa gat	1056
Ile Ile Lys Pro Ser Ala Gln Leu Gln Phe Thr Asp Leu Lys Glu Asp	
340 345 350	
cat cca tta gta aaa ata tcg aac aat act ata tct gct caa ggc tcg	1104
His Pro Leu Val Lys Ile Ser Asn Asn Thr Ile Ser Ala Gln Gly Ser	
355 360 365	
tcg tcg tcg tcg tta tca gcg tcg aaa aat gga ttt aat agt cat act	1152
Ser Ser Ser Ser Leu Ser Ala Ser Lys Asn Gly Phe Asn Ser His Thr	
370 375 380	
cac aat tca gga gtc att gat cca tca gca ctt ata gat ggg aaa att	1200
His Asn Ser Gly Val Ile Asp Pro Ser Ala Leu Ile Asp Gly Lys Ile	
385 390 395 400	
tat cag act gat tgg aat caa tta caa ggt act gaa cta ata ttt gat	1248
Tyr Gln Thr Asp Trp Asn Gln Leu Gln Gly Thr Glu Leu Ile Phe Asp	
405 410 415	
gaa aat ggt caa ttt ata ggc aag gtt aag gaa cat ttg act tgc aat	1296
Glu Asn Gly Gln Phe Ile Gly Lys Val Lys Glu His Leu Thr Cys Asn	
420 425 430	
aat aac aca aaa ttc aca tta aaa aag gca gaa gaa gta gaa caa ctt	1344
Asn Asn Thr Lys Phe Thr Leu Lys Lys Ala Glu Glu Val Glu Gln Leu	
435 440 445	
cgt tca gca gat gat tct atc atg gat ata gat caa gac tca caa gga	1392
Arg Ser Ala Asp Asp Ser Ile Met Asp Ile Asp Gln Asp Ser Gln Gly	
450 455 460	
caa caa cca gct aga agt cag ttc tta aaa aga gca att gtg gct gct	1440
Gln Gln Pro Ala Arg Ser Gln Phe Leu Lys Arg Ala Ile Val Ala Ala	
465 470 475 480	
aga gcc aaa ggt aa	1454
Arg Ala Lys Gly	

<210> 16

<211> 484

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence: Splice Variant

<400> 16

Met Thr Ile Glu Thr Ile Tyr Ile Ala Arg His Gly Tyr Arg Ser Asn

1

5

10

15

Trp Leu Pro Pro Pro His Pro Pro Asn Pro Thr Gly Ile Asp Ser Asp
 20 25 30
 Pro Ala Leu Ala Pro His Gly Val Glu Gln Ala Gln Gln Leu Ala Ala
 35 40 45
 Tyr Leu Thr Ser Leu Pro Thr His Glu Lys Pro Glu Phe Ile Ile Ala
 50 55 60
 Ser Pro Phe Tyr Arg Cys Ile Glu Thr Ser Arg Pro Ile Ala Glu Met
 65 70 75 80
 Leu Asp Leu Lys Ile Ala Leu Glu Arg Gly Val Gly Glu Trp Phe Arg
 85 90 95
 Lys Asn Arg Asp Thr Lys Pro Val Pro Gly Asp Tyr Thr Gln Leu Arg
 100 105 110
 Thr Phe Phe Asp Lys Leu Leu Ile Asp Glu Asp Thr Trp Pro Arg Asp
 115 120 125
 Asn Leu Asn Val Ile Pro Asn Ile Glu Gly Glu Asp Tyr Asp Glu Ile
 130 135 140
 Tyr Asp Arg Ala Lys Leu Phe Trp Lys Lys Phe Ile Pro Glu Phe Glu
 145 150 155 160
 Lys Lys Phe Pro Glu Ile Lys Asn Val Leu Ile Val Thr His Ala Ala
 165 170 175
 Thr Lys Ile Ala Leu Gly Ser Ala Leu Leu Gln Leu Lys Ser Val Thr
 180 185 190
 Asp Val Ile Asp Asp Asn Gln Thr Val Leu Arg Ala Gly Ala Cys Ser
 195 200 205
 Leu Ser Lys Phe Val Arg Asp Gly Glu Asp Lys Thr Asn His Thr Ile
 210 215 220
 Gln Trp Lys Ile Val Met Asn Gly Asn Cys Glu Phe Leu Thr Gln Gly
 225 230 235 240
 Glu Glu Met Asn Trp Asp Phe Arg Arg Gly Val Glu Ala Gly Ser Ala
 245 250 255
 Glu Asp Ile Ala Gln Arg Lys Ala Ala Ala Glu Ala Glu Ala Lys Ala
 260 265 270
 Leu Lys Lys Asn Glu Gln Thr Lys Ser Asp Gly Pro Ile Thr Glu Ser
 275 280 285
 Ala Thr Gly Ala Glu Ile Asp Gly Asn Glu Asp Glu Phe Glu Thr Phe
 290 295 300
 Tyr Val Thr Ile Asp Ile Pro Ser Ile Ser Asn Lys Ile Asp Asn Glu
 305 310 315 320

Glu Glu Pro Pro Ser Arg Thr Gly Gln Ala Pro Lys Phe Lys Asn Asn
 325 330 335
 Ile Ile Lys Pro Ser Ala Gln Leu Gln Phe Thr Asp Leu Lys Glu Asp
 340 345 350
 His Pro Leu Val Lys Ile Ser Asn Asn Thr Ile Ser Ala Gln Gly Ser
 355 360 365
 Ser Ser Ser Ser Leu Ser Ala Ser Lys Asn Gly Phe Asn Ser His Thr
 370 375 380
 His Asn Ser Gly Val Ile Asp Pro Ser Ala Leu Ile Asp Gly Lys Ile
 385 390 395 400
 Tyr Gln Thr Asp Trp Asn Gln Leu Gln Gly Thr Glu Leu Ile Phe Asp
 405 410 415
 Glu Asn Gly Gln Phe Ile Gly Lys Val Lys Glu His Leu Thr Cys Asn
 420 425 430
 Asn Asn Thr Lys Phe Thr Leu Lys Lys Ala Glu Glu Val Glu Gln Leu
 435 440 445
 Arg Ser Ala Asp Asp Ser Ile Met Asp Ile Asp Gln Asp Ser Gln Gly
 450 455 460
 Gln Gln Pro Ala Arg Ser Gln Phe Leu Lys Arg Ala Ile Val Ala Ala
 465 470 475 480
 Arg Ala Lys Gly

<210> 17
 <211> 2877
 <212> DNA
 <213> Candida albicans

<220>
 <221> CDS
 <222> (1)..(2874)

<220>
 <221> gene
 <222> (1)..(2874)
 <223> gene CaMR212

<400> 17
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 Met Asn Leu Phe Gln His Lys His Gln Lys Leu Ile Leu Gln Cys Tyr
 1 5 10 15
 cct gct ggg aaa gca gtg gac aaa aaa ccc aac tcg tcc gag tta agt 96
 Pro Ala Gly Lys Ala Val Asp Lys Lys Pro Asn Ser Ser Glu Leu Ser
 20 25 30

tat tta tta tac tat gca tcc act cgt aga gtc aaa tta gaa aag gtg	144
Tyr Leu Leu Tyr Tyr Ala Ser Thr Arg Arg Val Lys Leu Glu Lys Val	
35 40 45	
att aat ttt ttg aaa gat aaa act cat cat gat gtt ggt aga aac cgt	192
Ile Asn Phe Leu Lys Asp Lys Thr His His Asp Val Gly Arg Asn Arg	
50 55 60	
act ggt aat tta caa gtc aca tta gcc att att cag gaa tta atc aaa	240
Thr Gly Asn Leu Gln Val Thr Leu Ala Ile Ile Gln Glu Leu Ile Lys	
65 70 75 80	
aaa tgt agt gaa aac ttg aat gtt ttt gcc ttt caa gtg tgc tat atc	288
Lys Cys Ser Glu Asn Leu Asn Val Phe Ala Phe Gln Val Cys Tyr Ile	
85 90 95	
ttg caa ctg att gcc aac act aag gat ctt gcc ttg tgt aaa aat gtt	336
Leu Gln Leu Ile Ala Asn Thr Lys Asp Leu Ala Leu Cys Lys Asn Val	
100 105 110	
gtc aaa aca ttt ggt gtt ttg tgt gaa aac ttg gat ggt ggg ttg ttc	384
Val Lys Thr Phe Gly Val Leu Cys Glu Asn Leu Asp Gly Gly Leu Phe	
115 120 125	
aca ggt gat aag gag ttt ata aag att ttc act gaa gtt ttc caa aca	432
Thr Gly Asp Lys Glu Phe Ile Lys Ile Phe Thr Glu Val Phe Gln Thr	
130 135 140	
tta gtt tcc ttt ggt aag gac aga tcg ggt gtt act cag tat gat tgg	480
Leu Val Ser Phe Gly Lys Asp Arg Ser Gly Val Thr Gln Tyr Asp Trp	
145 150 155 160	
cag atg att tct tta atg gct ata aat gat ata tcc agt tgt ttg agt	528
Gln Met Ile Ser Leu Met Ala Ile Asn Asp Ile Ser Ser Cys Leu Ser	
165 170 175	
tat aat gca gct gtt ggt aaa aag ttt att gct ttg tcg att cct gtt	576
Tyr Asn Ala Ala Val Gly Lys Lys Phe Ile Ala Leu Ser Ile Pro Val	
180 185 190	
tta ctt cag ttt att att gca aac aac cca caa agc agc ata ttg caa	624
Leu Leu Gln Phe Ile Ile Ala Asn Asn Pro Gln Ser Ser Ile Leu Gln	
195 200 205	
aga ttg aaa tcg aat ctc cac gtt gaa gat gat ggg aag agg ttg tca	672
Arg Leu Lys Ser Asn Leu His Val Glu Asp Asp Gly Lys Arg Leu Ser	
210 215 220	
cgt gct cat ctg caa aaa tcc cat agc aaa att gcc caa caa att gat	720
Arg Ala His Leu Gln Lys Ser His Ser Lys Ile Ala Gln Gln Ile Asp	
225 230 235 240	
gat gat ttc acc aat gat tct tta acc ttg aca gat atc act gaa aag	768
Asp Asp Phe Thr Asn Asp Ser Leu Thr Leu Thr Asp Ile Thr Glu Lys	
245 250 255	
gca ttt tcg tcg atg aaa tct ttt ttc aat acc aat gct gcc agt caa	816

Ala Phe Ser Ser Met Lys Ser Phe Phe Asn Thr Asn Ala Ala Ser Gln	
260 265 270	
atc tct gaa gtg aca aga gct gtt gtc caa cac aat att ctc aat gga	864
Ile Ser Glu Val Thr Arg Ala Val Val Gln His Asn Ile Leu Asn Gly	
275 280 285	
acc gat ttg gag tgg gga gtc tca ttc ttg gaa tta tgt att act tgg	912
Thr Asp Leu Glu Trp Gly Val Ser Phe Leu Glu Leu Cys Ile Thr Trp	
290 295 300	
att cca gtt caa tta cgt ttt gtc agt ttg tcc acc ttg ttg gcc act	960
Ile Pro Val Gln Leu Arg Phe Val Ser Leu Ser Thr Leu Leu Ala Thr	
305 310 315 320	
tta ggt aga att aat att gaa ggt aac acc aaa tcc aat tac aac atg	1008
Leu Gly Arg Ile Asn Ile Glu Gly Asn Thr Lys Ser Asn Tyr Asn Met	
325 330 335	
caa ttc cag tat gct cgt tac ttg tta gga tta ctt tca tct cgt gtg	1056
Gln Phe Gln Tyr Ala Arg Tyr Leu Leu Gly Leu Leu Ser Ser Arg Val	
340 345 350	
aac atg att ggg tta tca gtt tca gat att att caa cag ttg tta tcg	1104
Asn Met Ile Gly Leu Ser Val Ser Asp Ile Ile Gln Gln Leu Leu Ser	
355 360 365	
ttg caa gct gat ttg att ttg aag gca agt gat ttg gac aaa agt gaa	1152
Leu Gln Ala Asp Leu Ile Leu Lys Ala Ser Asp Leu Asp Lys Ser Glu	
370 375 380	
att tca att tta aca gac att tat tct gac tgt att tgt agt ttg act	1200
Ile Ser Ile Leu Thr Asp Ile Tyr Ser Asp Cys Ile Cys Ser Leu Thr	
385 390 395 400	
aca cat ata tat tac ttt gat caa gtc ccg gac tcg att caa gaa atc	1248
Thr His Ile Tyr Tyr Phe Asp Gln Val Pro Asp Ser Ile Gln Glu Ile	
405 410 415	
tta atc aag att gat tac att tta gaa agc agt ttt gtg gaa gat aat	1296
Leu Ile Lys Ile Asp Tyr Ile Leu Glu Ser Ser Phe Val Glu Asp Asn	
420 425 430	
aac att acg tcc act gga gaa caa att caa gat ttg att atc caa ttg	1344
Asn Ile Thr Ser Thr Gly Glu Gln Ile Gln Asp Leu Ile Ile Gln Leu	
435 440 445	
ttg gat aac att tcg aag att ttt tta att ttg aag aat aaa tca agc	1392
Leu Asp Asn Ile Ser Lys Ile Phe Leu Ile Leu Lys Asn Lys Ser Ser	
450 455 460	
tca att aat cgt aac cat gtg aat ttg gaa cat tgg gat atc agt tta	1440
Ser Ile Asn Arg Asn His Val Asn Leu Glu His Trp Asp Ile Ser Leu	
465 470 475 480	
gga tta ttg gct cca caa ggc gac cat gat gat aac aga aaa atg att	1488
Gly Leu Leu Ala Pro Gln Gly Asp His Asp Asp Asn Arg Lys Met Ile	

485

490

495

att tct acg aca caa ctt atc aat atc caa gcc agg tac ttg aaa gtg	1536
Ile Ser Thr Thr Gln Leu Ile Asn Ile Gln Ala Arg Tyr Leu Lys Val	
500 505 510	
ttt gat gag ttt ttg aat aat gaa ttg gcg gtt ggc aat tct aaa aag	1584
Phe Asp Glu Phe Leu Asn Asn Glu Leu Ala Val Gly Asn Ser Lys Lys	
515 520 525	
agc tat gat ctt ctt agc aaa cag tct cgt ttg gat cct gga agt aca	1632
Ser Tyr Asp Leu Leu Ser Lys Gln Ser Arg Leu Asp Pro Gly Ser Thr	
530 535 540	
gct gtt gaa gga gtg aac aag tct gac gat ctg gac aat ggt aag gac	1680
Ala Val Glu Gly Val Asn Lys Ser Asp Asp Leu Asp Asn Gly Lys Asp	
545 550 555 560	
ttt aaa aaa cct gat gcc aat caa tac att acc aat caa caa aac ttc	1728
Phe Lys Lys Pro Asp Ala Asn Gln Tyr Ile Thr Asn Gln Gln Asn Phe	
565 570 575	
ata tcc cat ttc ctt atg tat atc gac aaa ttt ttc gaa aat tac gat	1776
Ile Ser His Phe Leu Met Tyr Ile Asp Lys Phe Phe Glu Asn Tyr Asp	
580 585 590	
tcc ccc aac aca caa tca gtg tta ctt ttg gtt act gtt tta aaa gat	1824
Ser Pro Asn Thr Gln Ser Val Leu Leu Leu Val Thr Val Leu Lys Asp	
595 600 605	
atg atg aac att tta gga ttg aat ttc ttg agt aat ttt att cca ttt	1872
Met Met Asn Ile Leu Gly Leu Asn Phe Leu Ser Asn Phe Ile Pro Phe	
610 615 620	
ttc cac cat tgg gtt atg aaa gta aac aga gcc agt aat ttc act caa	1920
Phe His His Trp Val Met Lys Val Asn Arg Ala Ser Asn Phe Thr Gln	
625 630 635 640	
aga cag aaa ttc aaa gat act ttt gct cat att att tta tat tac atg	1968
Arg Gln Lys Phe Lys Asp Thr Phe Ala His Ile Ile Leu Tyr Tyr Met	
645 650 655	
ttg aaa gat ttg gat gag caa tat agt cat gat tta caa aat tat tgc	2016
Leu Lys Asp Leu Asp Glu Gln Tyr Ser His Asp Leu Gln Asn Tyr Cys	
660 665 670	
aaa agc tct aaa tta ttc aaa caa ata ttg gat gct gtt gaa tat aga	2064
Lys Ser Ser Lys Leu Phe Lys Gln Ile Leu Asp Ala Val Glu Tyr Arg	
675 680 685	
aaa atg caa aag ttt tgg gtc cat ggc att gac cct tca cca tct gat	2112
Lys Met Gln Lys Phe Trp Val His Gly Ile Asp Pro Ser Pro Ser Asp	
690 695 700	
ttg gaa aac act aaa ggc gac cgt acg ata ccc aca gat gcc aat ggt	2160
Leu Glu Asn Thr Lys Gly Asp Arg Thr Ile Pro Thr Asp Ala Asn Gly	
705 710 715 720	

aat tat att gct att aga atc aaa cct gaa aat att gag gaa ttt gcc	2208
Asn Tyr Ile Ala Ile Arg Ile Lys Pro Glu Asn Ile Glu Glu Phe Ala	
725 730 735	
tgt ggt aac aac ttt ttg att gta tgg tta cat ccc caa aaa caa tta	2256
Cys Gly Asn Asn Phe Leu Ile Val Trp Leu His Pro Gln Lys Gln Leu	
740 745 750	
ctc act gaa att gaa aaa tca caa gtc agt act cat atg agc aca ttc	2304
Leu Thr Glu Ile Glu Lys Ser Gln Val Ser Thr His Met Ser Thr Phe	
755 760 765	
aat aat gat tct aga aac aca aat atg aca gtg ata atg gat caa gga	2352
Asn Asn Asp Ser Arg Asn Thr Asn Met Thr Val Ile Met Asp Gln Gly	
770 775 780	
tca ctg gca cta agt gga ggt gca gac cat gga ggt cac ttt gtt ccg	2400
Ser Leu Ala Leu Ser Gly Gly Ala Asp His Gly Gly His Phe Val Pro	
785 790 795 800	
cca cct gaa ttt gtt aac cac acc ggt ttg tct tct gaa tct gcg tca	2448
Pro Pro Glu Phe Val Asn His Thr Gly Leu Ser Ser Glu Ser Ala Ser	
805 810 815	
tca aac tca gag aaa ggt ttg tat act ggt tta gga ttg ggt act gct	2496
Ser Asn Ser Glu Lys Gly Leu Tyr Thr Gly Leu Gly Leu Gly Thr Ala	
820 825 830	
ggg gat att act atg att cat tct gaa ata tta caa tac agt caa cat	2544
Gly Asp Ile Thr Met Ile His Ser Glu Ile Leu Gln Tyr Ser Gln His	
835 840 845	
ttc caa gaa aga ggt tta cct cat ggt aat ggg ttt gct act att tta	2592
Phe Gln Glu Arg Gly Leu Pro His Gly Asn Gly Phe Ala Thr Ile Leu	
850 855 860	
cga act gtc gat agt gtt aac agt act aat gat ggg tta att tat act	2640
Arg Thr Val Asp Ser Val Asn Ser Thr Asn Asp Gly Leu Ile Tyr Thr	
865 870 875 880	
tat gat agt aaa tat ttg caa tca cca aga gta agt gat ttg aaa gat	2688
Tyr Asp Ser Lys Tyr Leu Gln Ser Pro Arg Val Ser Asp Leu Lys Asp	
885 890 895	
gcc atg tca aca cat agg ggt ata agg tta tct aaa cca aat ttt ggt	2736
Ala Met Ser Thr His Arg Gly Ile Arg Leu Ser Lys Pro Asn Phe Gly	
900 905 910	
ggg gcc aat gga act gct aat atg acg gat tct gct tct aca tcc aat	2784
Gly Ala Asn Gly Thr Ala Asn Met Thr Asp Ser Ala Ser Thr Ser Asn	
915 920 925	
gga tct gtg ttg aat aaa aat atg caa act aca gat gtt gat tca att	2832
Gly Ser Val Leu Asn Lys Asn Met Gln Thr Thr Asp Val Asp Ser Ile	
930 935 940	

tta agt ggt ctt gaa agt gaa gac gaa gct gcg ttt gtt gtt taa
 Leu Ser Gly Leu Glu Ser Glu Asp Glu Ala Ala Phe Val Val
 945 950 955

2877

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 <212> PRT
 <213> Candida albicans

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 Pro Ala Gly Lys Ala Val Asp Lys Lys Pro Asn Ser Ser Glu Leu Ser
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 Tyr Leu Leu Tyr Tyr Ala Ser Thr Arg Arg Val Lys Leu Glu Lys Val
 35 40 45
 Ile Asn Phe Leu Lys Asp Lys Thr His His Asp Val Gly Arg Asn Arg
 50 55 60
 Thr Gly Asn Leu Gln Val Thr Leu Ala Ile Ile Gln Glu Leu Ile Lys
 65 70 75 80
 Lys Cys Ser Glu Asn Leu Asn Val Phe Ala Phe Gln Val Cys Tyr Ile
 85 90 95
 Leu Gln Leu Ile Ala Asn Thr Lys Asp Leu Ala Leu Cys Lys Asn Val
 100 105 110
 Val Lys Thr Phe Gly Val Leu Cys Glu Asn Leu Asp Gly Gly Leu Phe
 115 120 125
 Thr Gly Asp Lys Glu Phe Ile Lys Ile Phe Thr Glu Val Phe Gln Thr
 130 135 140
 Leu Val Ser Phe Gly Lys Asp Arg Ser Gly Val Thr Gln Tyr Asp Trp
 145 150 155 160
 Gln Met Ile Ser Leu Met Ala Ile Asn Asp Ile Ser Ser Cys Leu Ser
 165 170 175
 Tyr Asn Ala Ala Val Gly Lys Lys Phe Ile Ala Leu Ser Ile Pro Val
 180 185 190
 Leu Leu Gln Phe Ile Ile Ala Asn Asn Pro Gln Ser Ser Ile Leu Gln
 195 200 205
 Arg Leu Lys Ser Asn Leu His Val Glu Asp Asp Gly Lys Arg Leu Ser
 210 215 220
 Arg Ala His Leu Gln Lys Ser His Ser Lys Ile Ala Gln Gln Ile Asp
 225 230 235 240
 Asp Asp Phe Thr Asn Asp Ser Leu Thr Leu Thr Asp Ile Thr Glu Lys

245

250

255

Ala Phe Ser Ser Met Lys Ser Phe Phe Asn Thr Asn Ala Ala Ser Gln		
260	265	270
Ile Ser Glu Val Thr Arg Ala Val Val Gln His Asn Ile Leu Asn Gly		
275	280	285
Thr Asp Leu Glu Trp Gly Val Ser Phe Leu Glu Leu Cys Ile Thr Trp		
290	295	300
Ile Pro Val Gln Leu Arg Phe Val Ser Leu Ser Thr Leu Leu Ala Thr		
305	310	315
Leu Gly Arg Ile Asn Ile Glu Gly Asn Thr Lys Ser Asn Tyr Asn Met		
	325	330
Gln Phe Gln Tyr Ala Arg Tyr Leu Leu Gly Leu Leu Ser Ser Arg Val		
	340	345
Asn Met Ile Gly Leu Ser Val Ser Asp Ile Ile Gln Gln Leu Leu Ser		
	355	360
Leu Gln Ala Asp Leu Ile Leu Lys Ala Ser Asp Leu Asp Lys Ser Glu		
	370	375
Ile Ser Ile Leu Thr Asp Ile Tyr Ser Asp Cys Ile Cys Ser Leu Thr		
385	390	395
Thr His Ile Tyr Tyr Phe Asp Gln Val Pro Asp Ser Ile Gln Glu Ile		
	405	410
Leu Ile Lys Ile Asp Tyr Ile Leu Glu Ser Ser Phe Val Glu Asp Asn		
	420	425
Asn Ile Thr Ser Thr Gly Glu Gln Ile Gln Asp Leu Ile Ile Gln Leu		
	435	440
Leu Asp Asn Ile Ser Lys Ile Phe Leu Ile Leu Lys Asn Lys Ser Ser		
	450	455
Ser Ile Asn Arg Asn His Val Asn Leu Glu His Trp Asp Ile Ser Leu		
465	470	475
Gly Leu Leu Ala Pro Gln Gly Asp His Asp Asp Asn Arg Lys Met Ile		
	485	490
Ile Ser Thr Thr Gln Leu Ile Asn Ile Gln Ala Arg Tyr Leu Lys Val		
	500	505
Phe Asp Glu Phe Leu Asn Asn Glu Leu Ala Val Gly Asn Ser Lys Lys		
	515	520
Ser Tyr Asp Leu Leu Ser Lys Gln Ser Arg Leu Asp Pro Gly Ser Thr		
	530	540
Ala Val Glu Gly Val Asn Lys Ser Asp Asp Leu Asp Asn Gly Lys Asp		

545 550 555 560
 Phe Lys Lys Pro Asp Ala Asn Gln Tyr Ile Thr Asn Gln Gln Asn Phe
 565 570 575
 Ile Ser His Phe Leu Met Tyr Ile Asp Lys Phe Phe Glu Asn Tyr Asp
 580 585 590
 Ser Pro Asn Thr Gln Ser Val Leu Leu Val Thr Val Leu Lys Asp
 595 600 605
 Met Met Asn Ile Leu Gly Leu Asn Phe Leu Ser Asn Phe Ile Pro Phe
 610 615 620
 Phe His His Trp Val Met Lys Val Asn Arg Ala Ser Asn Phe Thr Gln
 625 630 635 640
 Arg Gln Lys Phe Lys Asp Thr Phe Ala His Ile Ile Leu Tyr Tyr Met
 645 650 655
 Leu Lys Asp Leu Asp Glu Gln Tyr Ser His Asp Leu Gln Asn Tyr Cys
 660 665 670
 Lys Ser Ser Lys Leu Phe Lys Gln Ile Leu Asp Ala Val Glu Tyr Arg
 675 680 685
 Lys Met Gln Lys Phe Trp Val His Gly Ile Asp Pro Ser Pro Ser Asp
 690 695 700
 Leu Glu Asn Thr Lys Gly Asp Arg Thr Ile Pro Thr Asp Ala Asn Gly
 705 710 715 720
 Asn Tyr Ile Ala Ile Arg Ile Lys Pro Glu Asn Ile Glu Glu Phe Ala
 725 730 735
 Cys Gly Asn Asn Phe Leu Ile Val Trp Leu His Pro Gln Lys Gln Leu
 740 745 750
 Leu Thr Glu Ile Glu Lys Ser Gln Val Ser Thr His Met Ser Thr Phe
 755 760 765
 Asn Asn Asp Ser Arg Asn Thr Asn Met Thr Val Ile Met Asp Gln Gly
 770 775 780
 Ser Leu Ala Leu Ser Gly Gly Ala Asp His Gly Gly His Phe Val Pro
 785 790 795 800
 Pro Pro Glu Phe Val Asn His Thr Gly Leu Ser Ser Glu Ser Ala Ser
 805 810 815
 Ser Asn Ser Glu Lys Gly Leu Tyr Thr Gly Leu Gly Leu Gly Thr Ala
 820 825 830
 Gly Asp Ile Thr Met Ile His Ser Glu Ile Leu Gln Tyr Ser Gln His
 835 840 845
 Phe Gln Glu Arg Gly Leu Pro His Gly Asn Gly Phe Ala Thr Ile Leu

850

855

860

Arg Thr Val Asp Ser Val Asn Ser Thr Asn Asp Gly Leu Ile Tyr Thr
 865 870 875 880

Tyr Asp Ser Lys Tyr Leu Gln Ser Pro Arg Val Ser Asp Leu Lys Asp
 885 890 895

Ala Met Ser Thr His Arg Gly Ile Arg Leu Ser Lys Pro Asn Phe Gly
 900 905 910

Gly Ala Asn Gly Thr Ala Asn Met Thr Asp Ser Ala Ser Thr Ser Asn
 915 920 925

Gly Ser Val Leu Asn Lys Asn Met Gln Thr Thr Asp Val Asp Ser Ile
 930 935 940

Leu Ser Gly Leu Glu Ser Glu Asp Glu Ala Ala Phe Val Val
 945 950 955

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<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Homologous
 Fragment to Sc YMR212c

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 aaaggcaaaa acattcaagt ttccactaca ttttttgatt aattcctgaa taatggctaa 180
 tgtgacttgt aaattaccag tacggtttct accaacaatca tgatgagttt tatctttcaa 240
 aaaattaatc accttttcta atttgactct acgagtggat gcatagtata ataaataact 300
 taactcggac gagttggggt tttgtccac tgctttccca gcaggataac attgtaatat 360
 taacttttga tgtttatggt gaaacaaatt cattcttgga tctggaagtt gaagaaacta 420
 ttgaatcaaa acaggattta attaaccaat agaaaagaag taactcttga gttaaaaagg 480
 atattcttga tgaaaaaag gagaaaaaag gggaaagaag actctgaaaa tgaattaaag 540
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<210> 20

<211> 3771

<212> DNA

<213> Candida albicans

<220>
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<220>
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 <223> gene CaDR325

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 1 5 10 15

act ttg gat gaa ata aaa tat gcc atg aaa cat gtt ttc caa gat gct 96
 Thr Leu Asp Glu Ile Lys Tyr Ala Met Lys His Val Phe Gln Asp Ala
 20 25 30

caa tta ggt tta gca gga cat aga aaa tta gtg gta att ttg aaa aat 144
 Gln Leu Gly Leu Ala Gly His Arg Lys Leu Val Val Ile Leu Lys Asn
 35 40 45

gta ttt aaa aaa gcc att gaa tta aat caa att aat ttc ttt gcc atg 192
 Val Phe Lys Lys Ala Ile Glu Leu Asn Gln Ile Asn Phe Phe Ala Met
 50 55 60

tgt ttt act aaa ttg tta tct aaa gta tta cct ttg aaa aga gga gtt 240
 Cys Phe Thr Lys Leu Leu Ser Lys Val Leu Pro Leu Lys Arg Gly Val
 65 70 75 80

ttg gca ggt gat aga ata gtc aaa ttt tgt tat ctg ttt gtt aat ggt 288
 Leu Ala Gly Asp Arg Ile Val Lys Phe Cys Tyr Leu Phe Val Asn Gly
 85 90 95

ctt gta aaa gat gcc aat gaa gaa aaa cgt tcc aaa gaa gaa gaa aaa 336
 Leu Val Lys Asp Ala Asn Glu Glu Lys Arg Ser Lys Glu Glu Glu Lys
 100 105 110

gaa gaa aaa gac aaa gac gaa gac aaa gat acg aat gaa agt gat aaa 384
 Glu Glu Lys Asp Lys Asp Glu Asp Lys Asp Thr Asn Glu Ser Asp Lys
 115 120 125

aat gaa gaa gat cag gaa gat caa gaa gga gaa gga gat caa gaa act 432
 Asn Glu Glu Asp Gln Glu Asp Gln Glu Gly Glu Gly Asp Gln Glu Thr
 130 135 140

cca att tcg gaa ttc ata tca tat ttg ata aaa tat tta ttg agt ggg 480
 Pro Ile Ser Glu Phe Ile Ser Tyr Leu Ile Lys Tyr Leu Leu Ser Gly
 145 150 155 160

ata gag gct aaa gat aaa ctg gtt cgt tat cgt gtt gta caa aca tta 528
 Ile Glu Ala Lys Asp Lys Leu Val Arg Tyr Arg Val Val Gln Thr Leu
 165 170 175

gca tac ttg gtt gaa ttc ttg acc gag ata cac gag aat aat aca ttg 576
 Ala Tyr Leu Val Glu Phe Leu Thr Glu Ile His Glu Asn Asn Thr Leu
 180 185 190

gaa gcg tta tat act tta tta agt aat agg cta caa gat aaa gag ctg	624
Glu Ala Leu Tyr Thr Leu Leu Ser Asn Arg Leu Gln Asp Lys Glu Leu	
195 200 205	
tcg ata cgt att caa gct gtt gtg gca tta tca cat ttt caa tta ttt	672
Ser Ile Arg Ile Gln Ala Val Val Ala Leu Ser His Phe Gln Leu Phe	
210 215 220	
gaa ttt agt att gaa ggt gat act gga gaa ttt gag gat gaa tta ata	720
Glu Phe Ser Ile Glu Gly Asp Thr Gly Glu Phe Glu Asp Glu Leu Ile	
225 230 235 240	
tca agt aac caa att cag aat aaa ttg ata aat tcc att caa aat gat	768
Ser Ser Asn Gln Ile Gln Asn Lys Leu Ile Asn Ser Ile Gln Asn Asp	
245 250 255	
gat agt cca gaa gtc aga cgt gca gca tta atg aat ttg gtt aaa aca	816
Asp Ser Pro Glu Val Arg Arg Ala Ala Leu Met Asn Leu Val Lys Thr	
260 265 270	
caa gat aca ata ccg att tta ctt gaa cga gcc aga gat tcc aat tct	864
Gln Asp Thr Ile Pro Ile Leu Leu Glu Arg Ala Arg Asp Ser Asn Ser	
275 280 285	
att aat aga aga ttg gtt tat tct aaa ata gct cgt gaa tta ata act	912
Ile Asn Arg Arg Leu Val Tyr Ser Lys Ile Ala Arg Glu Leu Ile Thr	
290 295 300	
gat ttg gat gat ctt gaa ttt gaa gat agg gaa ttt tta tta aaa tgg	960
Asp Leu Asp Asp Leu Glu Phe Glu Asp Arg Glu Phe Leu Leu Lys Trp	
305 310 315 320	
ggg tta aat gat cgt gat gaa act gtt aaa gca gcc gcc act aaa atg	1008
Gly Leu Asn Asp Arg Asp Glu Thr Val Lys Ala Ala Ala Thr Lys Met	
325 330 335	
ctt acc att tat tgg tat caa tct gtc aat gaa gat tta tta gaa tta	1056
Leu Thr Ile Tyr Trp Tyr Gln Ser Val Asn Glu Asp Leu Leu Glu Leu	
340 345 350	
att gat caa tta aat gtc aag agt gct ata gct gaa cag gcc ata tta	1104
Ile Asp Gln Leu Asn Val Lys Ser Ala Ile Ala Glu Gln Ala Ile Leu	
355 360 365	
gca ttt ttt aaa aat aaa cca gaa gtt ctt gaa act att aaa att gat	1152
Ala Phe Phe Lys Asn Lys Pro Glu Val Leu Glu Thr Ile Lys Ile Asp	
370 375 380	
gaa tca tat tgg aaa aat cta act aca gaa aag gca ttc ttg atg agg	1200
Glu Ser Tyr Trp Lys Asn Leu Thr Thr Glu Lys Ala Phe Leu Met Arg	
385 390 395 400	
acg ttt tat caa tat tgt aat gag aat caa tta cat gct tta atg gat	1248
Thr Phe Tyr Gln Tyr Cys Asn Glu Asn Gln Leu His Ala Leu Met Asp	
405 410 415	

gcc aat ttc cct gaa tta ctt gat ttg tca ata aca tta gaa aag tat 1296
 Ala Asn Phe Pro Glu Leu Leu Asp Leu Ser Ile Thr Leu Glu Lys Tyr
 420 425 430

ttg tca gtg agg ttg aaa act ata aat gaa aat gaa aat tta gtt aag 1344
 Leu Ser Val Arg Leu Lys Thr Ile Asn Glu Asn Glu Asn Leu Val Lys
 435 440 445

aca tgg gaa act tat aat gcc aag att gac gaa tta gat gat caa ata 1392
 Thr Trp Glu Thr Tyr Asn Ala Lys Ile Asp Glu Leu Asp Asp Gln Ile
 450 455 460

ttt agt ctt gaa aac cag att tcc aga ata aat act gat gcc gat aat 1440
 Phe Ser Leu Glu Asn Gln Ile Ser Arg Ile Asn Thr Asp Ala Asp Asn
 465 470 475 480

ttc cgt aaa agt tta tct aac att gaa gaa gat att att gaa atc aat 1488
 Phe Arg Lys Ser Leu Ser Asn Ile Glu Glu Asp Ile Ile Glu Ile Asn
 485 490 495

att gct aag gat ttg ttc aaa aag aga att aaa caa ttg aaa aac aac 1536
 Ile Ala Lys Asp Leu Phe Lys Lys Arg Ile Lys Gln Leu Lys Asn Asn
 500 505 510

agt ggg aat cta gaa gat ttg att act gaa gaa aat caa gag att gct 1584
 Ser Gly Asn Leu Glu Asp Leu Ile Thr Glu Glu Asn Gln Glu Ile Ala
 515 520 525

gat caa atc aag gat ttc ctg atg gaa gat ttg caa caa caa ttg gaa 1632
 Asp Gln Ile Lys Asp Phe Leu Met Glu Asp Leu Gln Gln Gln Leu Glu
 530 535 540

gat atc aat aaa aat ctt gat gaa att gaa cat cat cca gaa gat ata 1680
 Asp Ile Asn Lys Asn Leu Asp Glu Ile Glu His His Pro Glu Asp Ile
 545 550 555 560

acg gct aaa tta gaa gaa ctt caa aca aaa tat gat tct tgt att agg 1728
 Thr Ala Lys Leu Glu Glu Leu Gln Thr Lys Tyr Asp Ser Cys Ile Arg
 565 570 575

gcg ctt gaa acc act agt gaa ttg aaa att cag act gtt caa atc ttt 1776
 Ala Leu Glu Thr Thr Ser Glu Leu Lys Ile Gln Thr Val Gln Ile Phe
 580 585 590

gaa caa gaa cat gaa aat gat tgt atc ccc ttt gta gat gct ttg aaa 1824
 Glu Gln Glu His Glu Asn Asp Cys Ile Pro Phe Val Asp Ala Leu Lys
 595 600 605

gaa tta gaa ttc att att aat caa tta tta tta att gtt aaa gat ttt 1872
 Glu Leu Glu Phe Ile Ile Asn Gln Leu Leu Leu Ile Val Lys Asp Phe
 610 615 620

gat tat gga gat gaa atg gca aga aga aaa ttg tta cat ata ata aga 1920
 Asp Tyr Gly Asp Glu Met Ala Arg Arg Lys Leu Leu His Ile Ile Arg
 625 630 635 640

atg aca tta act gaa gat aaa tta cct gat gcg tta ata tca gtg gca 1968

Met Thr Leu Thr Glu Asp Lys Leu Pro Asp Ala Leu Ile Ser Val Ala	
645 650 655	
ctt aga gta tta cga gca ctt tct ata aat gaa aaa gat ttt gtt tcc	2016
Leu Arg Val Leu Arg Ala Leu Ser Ile Asn Glu Lys Asp Phe Val Ser	
660 665 670	
atg gcg gta gaa ata att act gat att cgt gat tct cga gat gat gaa	2064
Met Ala Val Glu Ile Ile Thr Asp Ile Arg Asp Ser Arg Asp Asp Glu	
675 680 685	
gag ttc cat tct gct gcc gct aca ttt gat gat gat gat gat gat att	2112
Glu Phe His Ser Ala Ala Ala Thr Phe Asp Asp Asp Asp Asp Asp Ile	
690 695 700	
ttg gga aat ggt gat gat gaa tct caa caa tca tca tca ctc agt gca	2160
Leu Gly Asn Gly Asp Asp Glu Ser Gln Gln Ser Ser Ser Leu Ser Ala	
705 710 715 720	
gta aca aag aag cga aga att gaa cca gat atg cca cca gat gat att	2208
Val Thr Lys Lys Arg Arg Ile Glu Pro Asp Met Pro Pro Asp Asp Ile	
725 730 735	
gtg tta aga tgt ctt acc atg aca caa tat gta ttg gaa gta att act	2256
Val Leu Arg Cys Leu Thr Met Thr Gln Tyr Val Leu Glu Val Ile Thr	
740 745 750	
cat agt ttg gat gat cat ctt tca ttg agt tct att tac agt ggt att	2304
His Ser Leu Asp Asp His Leu Ser Leu Ser Ser Ile Tyr Ser Gly Ile	
755 760 765	
gtc aat tat gct att cag aat gaa tcg aaa aag aaa tta tat ctt gct	2352
Val Asn Tyr Ala Ile Gln Asn Glu Ser Lys Lys Lys Leu Tyr Leu Ala	
770 775 780	
ggg tta act tgt tta gga ctt tat tct tta att gat tcc aaa att gcc	2400
Gly Leu Thr Cys Leu Gly Leu Tyr Ser Leu Ile Asp Ser Lys Ile Ala	
785 790 795 800	
aga att gca act aca aca tta tta ctg gca atg aga agt aat ggt gaa	2448
Arg Ile Ala Thr Thr Leu Leu Leu Ala Met Arg Ser Asn Gly Glu	
805 810 815	
gaa gtg aaa gag att gga atg aaa gct att gtg gat ata ttg gca att	2496
Glu Val Lys Glu Ile Gly Met Lys Ala Ile Val Asp Ile Leu Ala Ile	
820 825 830	
tat ggt atg agt att ctt gat aaa tca tct aaa tac aaa tat tca aga	2544
Tyr Gly Met Ser Ile Leu Asp Lys Ser Ser Lys Tyr Lys Tyr Ser Arg	
835 840 845	
atg ttt ttc aaa gtt tta aat tca ttt gat gca cca aaa tta caa tgc	2592
Met Phe Phe Lys Val Leu Asn Ser Phe Asp Ala Pro Lys Leu Gln Cys	
850 855 860	
att gtc gct gaa gga tta tgc aaa ttg ttt tta gcc gat att ttg tac	2640
Ile Val Ala Glu Gly Leu Cys Lys Leu Phe Leu Ala Asp Ile Leu Tyr	

865	870	875	880	
aag act gac aaa cgg agt tta ttt gga aat gct att caa ggt ggt ggt				2688
Lys Thr Asp Lys Arg Ser Leu Phe Gly Asn Ala Ile Gln Gly Gly Gly	885	890	895	
ggt ggt ggt ggt ggt aat gat gat cca act acc acc aat gac gat gaa				2736
Gly Gly Gly Gly Gly Asn Asp Asp Pro Thr Thr Thr Asn Asp Asp Glu	900	905	910	
act gaa gaa gaa aca gat cga gag cat gaa aag cat tta ttt gaa gcg				2784
Thr Glu Glu Glu Thr Asp Arg Glu His Glu Lys His Leu Phe Glu Ala	915	920	925	
att gta ctt att tat ttc aac ccc aac acc aaa tca aat caa gaa tta				2832
Ile Val Leu Ile Tyr Phe Asn Pro Asn Thr Lys Ser Asn Gln Glu Leu	930	935	940	
caa caa att ttg tca ttt tgt att cca gtt tat gcc ttt tct cat ata				2880
Gln Gln Ile Leu Ser Phe Cys Ile Pro Val Tyr Ala Phe Ser His Ile	945	950	955	960
aat cat caa atc aat tta gct gca gtt agt ggt gat gtt att tat cga				2928
Asn His Gln Ile Asn Leu Ala Ala Val Ser Gly Asp Val Ile Tyr Arg	965	970	975	
ctt ttc act gaa aca gaa aca gaa tta tca cca agt gtt ata atc cct				2976
Leu Phe Thr Glu Thr Glu Thr Glu Leu Ser Pro Ser Val Ile Ile Pro	980	985	990	
caa tta ata tca tgg tgt gat cct cga aat tta gtt aaa tta tcg aat				3024
Gln Leu Ile Ser Trp Cys Asp Pro Arg Asn Leu Val Lys Leu Ser Asn	995	1000	1005	
gag gaa ata aat caa gca aca tca cat tta tgg caa tgt gtt tat tta				3072
Glu Glu Ile Asn Gln Ala Thr Ser His Leu Trp Gln Cys Val Tyr Leu	1010	1015	1020	
tta caa gtg gtt gaa caa gta gat gct cgt aat gtt aaa aga tgc atc				3120
Leu Gln Val Val Glu Gln Val Asp Ala Arg Asn Val Lys Arg Cys Ile	1025	1030	1035	1040
att aac aat ttg aat aaa ttt cat ata acg gaa gaa tta gag tca aat				3168
Ile Asn Asn Leu Asn Lys Phe His Ile Thr Glu Glu Leu Glu Ser Asn	1045	1050	1055	
caa tta caa gct tta att aaa gct ctt gat gct aca gtt gaa tta ttt				3216
Gln Leu Gln Ala Leu Ile Lys Ala Leu Asp Ala Thr Val Glu Leu Phe	1060	1065	1070	
act aat aat gaa gat aac cct aat ttt atc ttg gat aaa cca aca aag				3264
Thr Asn Asn Glu Asp Asn Pro Asn Phe Ile Leu Asp Lys Pro Thr Lys	1075	1080	1085	
aag aat ttt gat act ttt att gaa tca ata aag aat aaa ttg gaa att				3312
Lys Asn Phe Asp Thr Phe Ile Glu Ser Ile Lys Asn Lys Leu Glu Ile	1090	1095	1100	

gct caa aaa aga gaa gaa aat gaa ctg att aaa agt ggt aca aat tca 3360
 Ala Gln Lys Arg Glu Glu Asn Glu Leu Ile Lys Ser Gly Thr Asn Ser
 1105 1110 1115 1120

ata tta cat gaa tta gat gat tta gat att gga act gga gag agt agt 3408
 Ile Leu His Glu Leu Asp Asp Leu Asp Ile Gly Thr Gly Glu Ser Ser
 1125 1130 1135

caa ata tct ata aaa tca gaa aca aaa aga aga gat ctg gat cga tct 3456
 Gln Ile Ser Ile Lys Ser Glu Thr Lys Arg Arg Asp Leu Asp Arg Ser
 1140 1145 1150

ctg caa gtt agt aaa act acg tca cca gaa act tca gaa aat gaa gat 3504
 Leu Gln Val Ser Lys Thr Thr Ser Pro Glu Thr Ser Glu Asn Glu Asp
 1155 1160 1165

gaa gag gat gat aat gag gag gag gaa caa gag aag aag aaa agt ttt 3552
 Glu Glu Asp Asp Asn Glu Glu Glu Glu Gln Glu Lys Lys Lys Ser Phe
 1170 1175 1180

act gat gga aaa aat aaa ctt gaa cta aag gca gat aag cca atc aca 3600
 Thr Asp Gly Lys Asn Lys Leu Glu Leu Lys Ala Asp Lys Pro Ile Thr
 1185 1190 1195 1200

ttt aaa gct gaa gac aag agg gaa ggg tca gtt gaa aca gat cat ggt 3648
 Phe Lys Ala Glu Asp Lys Arg Glu Gly Ser Val Glu Thr Asp His Gly
 1205 1210 1215

caa gaa caa gtt cta gtt gaa tca aag aaa gtc att gat agt aat gtt 3696
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 1220 1225 1230

gaa gat tct tta gaa gat ata gat aag ttt tta gaa gaa gca gat gat 3744
 Glu Asp Ser Leu Glu Asp Ile Asp Lys Phe Leu Glu Glu Ala Asp Asp
 1235 1240 1245

gtt gat tat ggt gat att tca atg gat 3771
 Val Asp Tyr Gly Asp Ile Ser Met Asp
 1250 1255

<210> 21

<211> 1257

<212> PRT

<213> Candida albicans

<400> 21

Met Asp Ile Pro Pro Lys Pro Thr Leu Lys Ala Ile Lys Lys Phe Arg
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Thr Leu Asp Glu Ile Lys Tyr Ala Met Lys His Val Phe Gln Asp Ala
 20 25 30

Gln Leu Gly Leu Ala Gly His Arg Lys Leu Val Val Ile Leu Lys Asn
 35 40 45

Val Phe Lys Lys Ala Ile Glu Leu Asn Gln Ile Asn Phe Phe Ala Met
 50 55 60
 Cys Phe Thr Lys Leu Leu Ser Lys Val Leu Pro Leu Lys Arg Gly Val
 65 70 75 80
 Leu Ala Gly Asp Arg Ile Val Lys Phe Cys Tyr Leu Phe Val Asn Gly
 85 90 95
 Leu Val Lys Asp Ala Asn Glu Glu Lys Arg Ser Lys Glu Glu Glu Lys
 100 105 110
 Glu Glu Lys Asp Lys Asp Glu Asp Lys Asp Thr Asn Glu Ser Asp Lys
 115 120 125
 Asn Glu Glu Asp Gln Glu Asp Gln Glu Gly Glu Gly Asp Gln Glu Thr
 130 135 140
 Pro Ile Ser Glu Phe Ile Ser Tyr Leu Ile Lys Tyr Leu Leu Ser Gly
 145 150 155 160
 Ile Glu Ala Lys Asp Lys Leu Val Arg Tyr Arg Val Val Gln Thr Leu
 165 170 175
 Ala Tyr Leu Val Glu Phe Leu Thr Glu Ile His Glu Asn Asn Thr Leu
 180 185 190
 Glu Ala Leu Tyr Thr Leu Leu Ser Asn Arg Leu Gln Asp Lys Glu Leu
 195 200 205
 Ser Ile Arg Ile Gln Ala Val Val Ala Leu Ser His Phe Gln Leu Phe
 210 215 220
 Glu Phe Ser Ile Glu Gly Asp Thr Gly Glu Phe Glu Asp Glu Leu Ile
 225 230 235 240
 Ser Ser Asn Gln Ile Gln Asn Lys Leu Ile Asn Ser Ile Gln Asn Asp
 245 250 255
 Asp Ser Pro Glu Val Arg Arg Ala Ala Leu Met Asn Leu Val Lys Thr
 260 265 270
 Gln Asp Thr Ile Pro Ile Leu Leu Glu Arg Ala Arg Asp Ser Asn Ser
 275 280 285
 Ile Asn Arg Arg Leu Val Tyr Ser Lys Ile Ala Arg Glu Leu Ile Thr
 290 295 300
 Asp Leu Asp Asp Leu Glu Phe Glu Asp Arg Glu Phe Leu Leu Lys Trp
 305 310 315 320
 Gly Leu Asn Asp Arg Asp Glu Thr Val Lys Ala Ala Ala Thr Lys Met
 325 330 335
 Leu Thr Ile Tyr Trp Tyr Gln Ser Val Asn Glu Asp Leu Leu Glu Leu
 340 345 350

Ile Asp Gln Leu Asn Val Lys Ser Ala Ile Ala Glu Gln Ala Ile Leu
 355 360 365
 Ala Phe Phe Lys Asn Lys Pro Glu Val Leu Glu Thr Ile Lys Ile Asp
 370 375 380
 Glu Ser Tyr Trp Lys Asn Leu Thr Thr Glu Lys Ala Phe Leu Met Arg
 385 390 395 400
 Thr Phe Tyr Gln Tyr Cys Asn Glu Asn Gln Leu His Ala Leu Met Asp
 405 410 415
 Ala Asn Phe Pro Glu Leu Leu Asp Leu Ser Ile Thr Leu Glu Lys Tyr
 420 425 430
 Leu Ser Val Arg Leu Lys Thr Ile Asn Glu Asn Glu Asn Leu Val Lys
 435 440 445
 Thr Trp Glu Thr Tyr Asn Ala Lys Ile Asp Glu Leu Asp Asp Gln Ile
 450 455 460
 Phe Ser Leu Glu Asn Gln Ile Ser Arg Ile Asn Thr Asp Ala Asp Asn
 465 470 475 480
 Phe Arg Lys Ser Leu Ser Asn Ile Glu Glu Asp Ile Ile Glu Ile Asn
 485 490 495
 Ile Ala Lys Asp Leu Phe Lys Lys Arg Ile Lys Gln Leu Lys Asn Asn
 500 505 510
 Ser Gly Asn Leu Glu Asp Leu Ile Thr Glu Glu Asn Gln Glu Ile Ala
 515 520 525
 Asp Gln Ile Lys Asp Phe Leu Met Glu Asp Leu Gln Gln Gln Leu Glu
 530 535 540
 Asp Ile Asn Lys Asn Leu Asp Glu Ile Glu His His Pro Glu Asp Ile
 545 550 555 560
 Thr Ala Lys Leu Glu Glu Leu Gln Thr Lys Tyr Asp Ser Cys Ile Arg
 565 570 575
 Ala Leu Glu Thr Thr Ser Glu Leu Lys Ile Gln Thr Val Gln Ile Phe
 580 585 590
 Glu Gln Glu His Glu Asn Asp Cys Ile Pro Phe Val Asp Ala Leu Lys
 595 600 605
 Glu Leu Glu Phe Ile Ile Asn Gln Leu Leu Leu Ile Val Lys Asp Phe
 610 615 620
 Asp Tyr Gly Asp Glu Met Ala Arg Arg Lys Leu Leu His Ile Ile Arg
 625 630 635 640
 Met Thr Leu Thr Glu Asp Lys Leu Pro Asp Ala Leu Ile Ser Val Ala
 645 650 655

Leu Arg Val Leu Arg Ala Leu Ser Ile Asn Glu Lys Asp Phe Val Ser
 660 665 670
 Met Ala Val Glu Ile Ile Thr Asp Ile Arg Asp Ser Arg Asp Asp Glu
 675 680 685
 Glu Phe His Ser Ala Ala Ala Thr Phe Asp Asp Asp Asp Asp Ile
 690 695 700
 Leu Gly Asn Gly Asp Asp Glu Ser Gln Gln Ser Ser Ser Leu Ser Ala
 705 710 715 720
 Val Thr Lys Lys Arg Arg Ile Glu Pro Asp Met Pro Pro Asp Asp Ile
 725 730 735
 Val Leu Arg Cys Leu Thr Met Thr Gln Tyr Val Leu Glu Val Ile Thr
 740 745 750
 His Ser Leu Asp Asp His Leu Ser Leu Ser Ser Ile Tyr Ser Gly Ile
 755 760 765
 Val Asn Tyr Ala Ile Gln Asn Glu Ser Lys Lys Lys Leu Tyr Leu Ala
 770 775 780
 Gly Leu Thr Cys Leu Gly Leu Tyr Ser Leu Ile Asp Ser Lys Ile Ala
 785 790 795 800
 Arg Ile Ala Thr Thr Thr Leu Leu Leu Ala Met Arg Ser Asn Gly Glu
 805 810 815
 Glu Val Lys Glu Ile Gly Met Lys Ala Ile Val Asp Ile Leu Ala Ile
 820 825 830
 Tyr Gly Met Ser Ile Leu Asp Lys Ser Ser Lys Tyr Lys Tyr Ser Arg
 835 840 845
 Met Phe Phe Lys Val Leu Asn Ser Phe Asp Ala Pro Lys Leu Gln Cys
 850 855 860
 Ile Val Ala Glu Gly Leu Cys Lys Leu Phe Leu Ala Asp Ile Leu Tyr
 865 870 875 880
 Lys Thr Asp Lys Arg Ser Leu Phe Gly Asn Ala Ile Gln Gly Gly Gly
 885 890 895
 Gly Gly Gly Gly Gly Asn Asp Asp Pro Thr Thr Thr Asn Asp Asp Glu
 900 905 910
 Thr Glu Glu Glu Thr Asp Arg Glu His Glu Lys His Leu Phe Glu Ala
 915 920 925
 Ile Val Leu Ile Tyr Phe Asn Pro Asn Thr Lys Ser Asn Gln Glu Leu
 930 935 940
 Gln Gln Ile Leu Ser Phe Cys Ile Pro Val Tyr Ala Phe Ser His Ile
 945 950 955 960

Asn His Gln Ile Asn Leu Ala Ala Val Ser Gly Asp Val Ile Tyr Arg
 965 970 975
 Leu Phe Thr Glu Thr Glu Thr Glu Leu Ser Pro Ser Val Ile Ile Pro
 980 985 990
 Gln Leu Ile Ser Trp Cys Asp Pro Arg Asn Leu Val Lys Leu Ser Asn
 995 1000 1005
 Glu Glu Ile Asn Gln Ala Thr Ser His Leu Trp Gln Cys Val Tyr Leu
 1010 1015 1020
 Leu Gln Val Val Glu Gln Val Asp Ala Arg Asn Val Lys Arg Cys Ile
 025 1030 1035 1040
 Ile Asn Asn Leu Asn Lys Phe His Ile Thr Glu Glu Leu Glu Ser Asn
 1045 1050 1055
 Gln Leu Gln Ala Leu Ile Lys Ala Leu Asp Ala Thr Val Glu Leu Phe
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 Thr Asn Asn Glu Asp Asn Pro Asn Phe Ile Leu Asp Lys Pro Thr Lys
 1075 1080 1085
 Lys Asn Phe Asp Thr Phe Ile Glu Ser Ile Lys Asn Lys Leu Glu Ile
 1090 1095 1100
 Ala Gln Lys Arg Glu Glu Asn Glu Leu Ile Lys Ser Gly Thr Asn Ser
 105 1110 1115 1120
 Ile Leu His Glu Leu Asp Asp Leu Asp Ile Gly Thr Gly Glu Ser Ser
 1125 1130 1135
 Gln Ile Ser Ile Lys Ser Glu Thr Lys Arg Arg Asp Leu Asp Arg Ser
 1140 1145 1150
 Leu Gln Val Ser Lys Thr Thr Ser Pro Glu Thr Ser Glu Asn Glu Asp
 1155 1160 1165
 Glu Glu Asp Asp Asn Glu Glu Glu Glu Gln Glu Lys Lys Lys Ser Phe
 1170 1175 1180
 Thr Asp Gly Lys Asn Lys Leu Glu Leu Lys Ala Asp Lys Pro Ile Thr
 185 1190 1195 1200
 Phe Lys Ala Glu Asp Lys Arg Glu Gly Ser Val Glu Thr Asp His Gly
 1205 1210 1215
 Gln Glu Gln Val Leu Val Glu Ser Lys Lys Val Ile Asp Ser Asn Val
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 <211> 603
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Homologous
 Fragment to Sc YDR325

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 gatcaggaag atcaagaagg agaaggagat caagaaactc caatttcgga attcatatca 180
 tatttgataa aatatttatt gagtgggata gaggctaaag ataaactggt tcgttatcgt 240
 gttgtacaaa cattagcata cttggttgaa ttcttgaccg agatacacga gaataatata 300
 ttggaagcgt tatatacttt attaagtaat aggctacaag ataaagagct gtcgatacgt 360
 attcaagctg ttgtggcatt atcacatttt caattatttg aatttagtat tgaaggatgat 420
 actggagaat ttgaggatga attaatatca agtaacccaa ttcagaataa attgataaat 480
 tccattcaaa atgatgatag tccagaagtc agacgtgcag cattaatgaa ttgggttaaa 540
 acacaagata caataccgat ttacttgag cgagccagag attccaattc tattaataga 600
 aga 603

<210> 23
 <211> 581
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Homologous
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 tgctatagct gaacaggcca tattagcatt ttttaaaaat aaaccagaag ttcttgcaac 180
 tattaataatt gatgaatcat attggaaaaa tctaactaca gaaaaggcat tcttgatgag 240
 gacgttttat caatattgta atgagaatca attacatgct ttaatggatg ccaatttccc 300
 tgaattactt gatttgtcaa taacattaga aaagtatttg tcagtggagg tgaatacaat 360
 aatgaaaat gaaaatttaa ttaagacatg ggaaacttat aatgccaaaga ttgacgaatt 420

agatgatcaa atatttagtc ttgaaaacca gatttccaga ataaatactg atgccgataa 480
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<210> 24
 <211> 662
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Homologous
 Fragment to Sc YDR325

<400> 24
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 attcaagggtg gtggtggtgg tgatgatcca actaccacca atgacgatga aactgaagaa 180
 gaaacagatc gagagcatga aaagcattta tttgaagcga ttgtacttat ttatttcaac 240
 cccaacacca aatcaaatca agaattacaa caaattttgt catTTTgtat tccagtttat 300
 gccttttctc atataaatca tcaaatcaat ttagctgcag ttagtggtga tgttatttat 360
 cgacttttca ctgaaacaga aacagaatta tcaccaagtg ttataatccc tcaattaata 420
 tcatggtgtg atcctcgaaa tttagttaaa ttatcgatg aggaaataaa tcaagcaaca 480
 tcacatttat ggcaatgtgt ttatttatta caagtgttg aacaagtaga tgctcgtaat 540
 gttaaaagat gcatcattaa caatttgaat aaatttcata taacggaaga attagaatca 600
 aatcaattac aagctttaat taaagctctt gatgctacag ttgaattatt tactaataat 660
 ga 662

<210> 25
 <211> 231
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Homologous
 Fragment to Sc YOR110

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 gttaaaatca gttactgatg ttatagatga taatcaaact gtgttacgtg ctggtgcatg 120

ttcattatcc aaatttggtta gagatggcga agataaaacc aatcatacta ttcaatggaa 180
aattgtcatg aatggtaatt gtgaattctt gacacagggt gaagaaatga a 231

aaa gag att gga atg aaa gct att gtg gat ata ttg gca att 2496
Glu Val Lys Glu Ile Gly Met Lys Ala Ile Val Asp Ile Leu Ala Ile
820 825 830

tat ggt atg agt att ctt gat aaa tca tct aaa tac aaa tat tca aga 2544
Tyr Gly Met Ser Ile Leu Asp Lys Ser Ser Lys Tyr Lys Tyr Ser Arg
835 840 845

atg ttt ttc aaa gtt tta aat tca ttt gat gca cca aaa tta caa tgc 2592
Met Phe Phe Lys Val Leu Asn Ser Phe Asp Ala Pro Lys Leu Gln Cys
850 855 860

att gtc gct gaa gga tta tgc aaa ttg ttt tta gcc gat att ttg tac 2640
Ile Val Ala Glu Gly Leu Cys Lys Leu Phe Leu Ala Asp Ile Leu Tyr
865 870 875 880

aag act gac aaa cgg agt tta ttt gga aat gct att caa ggt ggt ggt 2688
Lys Thr Asp Lys Arg Ser Leu Phe Gly Asn Ala Ile Gln Gly Gly Gly
885 890 895

ggt ggt ggt ggt ggt aat gat gat cca act acc acc aat gac gat gaa 2736
Gly Gly Gly Gly Gly Asn Asp Asp Pro Thr Thr Thr Asn Asp Asp Glu
900 905 910

act gaa gaa gaa aca gat cga gag cat gaa aag cat tta ttt gaa gcg 2784
Thr Glu Glu Glu Thr Asp Arg Glu His Glu Lys His Leu Phe Glu Ala
915 920 925

att gta ctt att tat ttc aac ccc aac acc aaa tca aat caa gaa tta 2832
Ile Val Leu Ile Tyr Phe Asn Pro Asn Thr Lys Ser Asn Gln Glu Leu
930 935 940

caa caa att ttg tca ttt tgt att cca gtt tat gcc ttt tct cat ata 2880
Gln Gln Ile Leu Ser Phe Cys Ile Pro Val Tyr Ala Phe Ser His Ile
945 950 955 960

aat cat caa atc aat tta gct gca gtt agt ggt gat gtt att tat cga 2928
Asn His Gln Ile Asn Leu Ala Ala Val Ser Gly Asp Val Ile Tyr Arg
965 970 975

ctt ttc act gaa aca gaa aca gaa tta tca cca agt gtt ata atc cct 2976
Leu Phe Thr Glu Thr Glu Thr Glu Leu Ser Pro Ser Val Ile Ile Pro
980 985 990

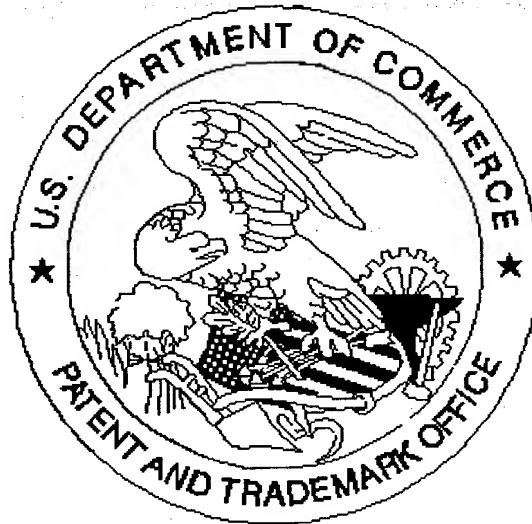
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Gln Leu Ile Ser Trp Cys Asp Pro Arg Asn Leu Val Lys Leu Ser Asn
995 1000 1005

gag gaa ata aat caa gca aca tca cat tta tgg caa tgt gtt tat tta 3072
Glu Glu Ile Asn Gln Ala Thr Ser His Leu Trp Gln Cys Val Tyr Leu
1010 1015 1020

tta caa gtg gtt gaa caa gta gat gct cgt aat gtt aaa aga tgc atc 3120
Leu Gln Val Val Glu Gln Val Asp Ala Arg Asn Val Lys Arg Cys Ile
1025 1030 1035 1040

att aac aat ttg a

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for scanning. (Document title)

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